Supporting Information

For

Development, Creation and Assessment of Novel Cathepsin C Inhibitors with Anti-inflammatory Properties

Xiaobao Shen[a], Nan Li[a], Miao Liu[a], Xuanzheng Han[a], Xinyu Zhang, Yazhi Wang, Jingwen Jia, Fufang Wu*[,a], Hongwei Chen*[,a] and Xinhua Liu*[,b]

[a] Medical School, Fuyang Normal University, Fuyang, 236037, China

[b] School of Pharmacy, Anhui Medical University, Hefei, 230032, China

*Email: wff03609344@126.com; chen790514@126.com; xhliuhx@163.com

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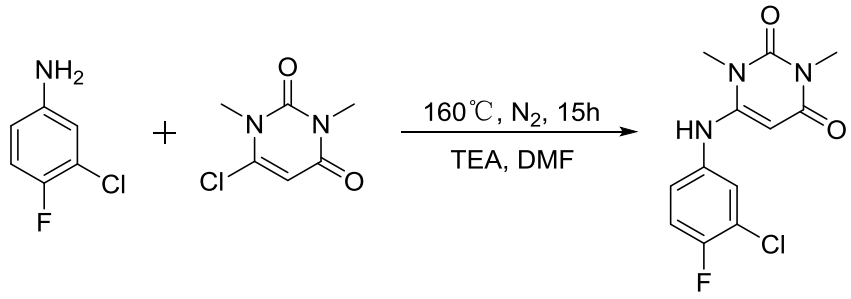
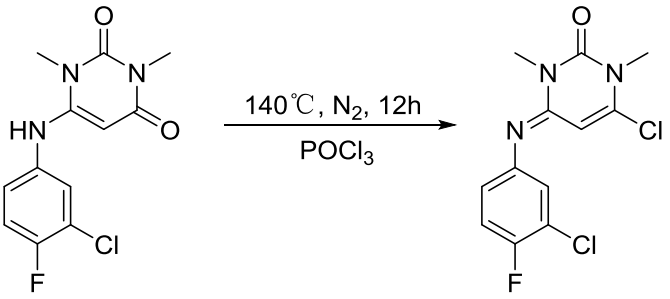
1. Chemistry Methods

General lnformation: Unless specified otherwise, all reactions were conducted in a pressure-resistant tube which was heated on a magnetic stirrer. The reagents and solvents used were obtained from commercial suppliers without further purification. NMR spectra (H, C, F) were measured using a Bruker Ascend 400 spectrometer and reported as chemical shifts in parts per million from residual solvent as an internal standard in $CDCl_3$, and coupling constant (J, hertz). High-resolution mass spectra (HR MS) were recorded on a Waters UPLC G2-Xs Qtof instrument.

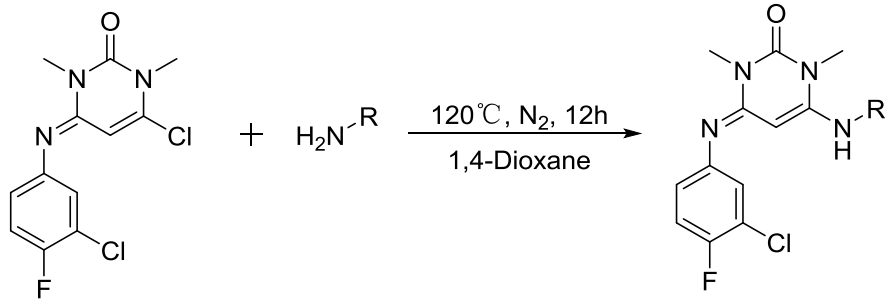
2. General procedure of reactions



Add 6-chloro-1,3-dimethyluracil (1 mmol, 0.2 g)), 3-chloro-4-fluoroaniline (2 mmol, 0.3 g), triethylamine (1.5 mmol, 0.2 mL), and DMF (5 mL) to the Schlenk tube and react for 15 hours under nitrogen protection at 160 ℃. The reaction mixture was then purified by column chromatography to yield the corresponding product **a** as yellow solid in 86% yield. (30:1 to 3:1 petroleum ether/ethyl acetate); mp 173-176 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (dd, *J* = 6.4, 2.4 Hz, 1H), 7.14 (t, *J* = 8.4 Hz, 1H), 7.10 – 6.97 (m, 1H), 4.85 (s, 1H), 3.53 (s, 3H), 3.28 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.7, 157.2, 156.6, 152.2, 147.8, 130.3 (d, *J* = 4.04 Hz), 129.3, 127.0 (d, *J* = 7.07 Hz), 118.3 (d, *J* = 23.23 Hz), 92.4, 35.7, 32.9.

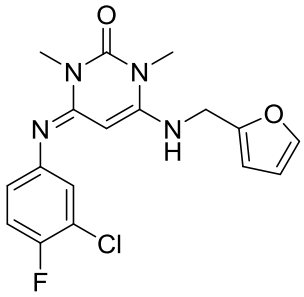


Add 6-(3-chloro-4-fluoroaniline)-1,3-dimethyl-2,4(1H,3H)-pyrimidinone (1 mmol, 0.3 g) and $POCl_3$ (3 mL) to the Schlenk tube and react for 12 hours under nitrogen protection at 140 ℃. The resulting solution was then dried by spinning, quenched with 1N ammonia water, and extracted three times with dichloromethane. The residue was subsequently purified by column chromatography to yield the corresponding product **b** as yellow solid with a ratio of 20:1-7:1 petroleum ether/ethyl acetate in 95% yield. mp 79-82 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 (t, *J* = 8.8 Hz, 1H), 6.83 (dd, *J* = 6.8, 2.8 Hz, 1H), 6.63 (ddd, *J* = 8.8, 4.0, 2.8 Hz, 1H), 5.67 (s, 1H), 3.50 (s, 3H), 3.43 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 155.6, 153.2, 151.1, 149.4, 145.9 (d, *J* = 3.03 Hz), 142.4, 123.4, 121.2 (q, *J* = 6.06 Hz), 117.0 (d, *J* = 21.21 Hz), 94.9, 33.3, 29.9.



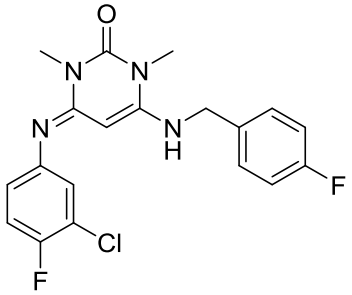
Add (E) -6-chloro-4- ((3-chloro-4-fluorophenyl) imino) -1,3-dimethyl-3,4-dihydropyrimidin-2 (1H) - one (1 mmol), amine compounds (2 mmol), and 1,4-dioxane (2.5 mL) to the Schlenk tube, and react for 12 hours under nitrogen protection. The reaction mixture was then purified by column chromatography to yield the corresponding product **1-36** (30:1 to 1:5 petroleum ether/ethyl acetate).

3. Characterization of products



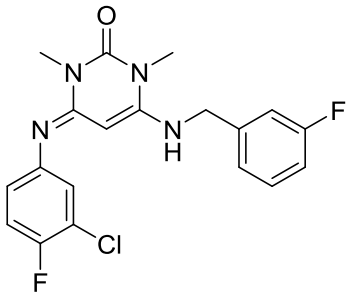
4.1.3.1-1

(E)-4-((3-chloro-4-fluorophenyl)imino)-6-((furan-2-ylmethyl)amino)-1,3-dimethyl-3,4-dihydropyrimidin-2(1H)-one (1). Product **1** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (326 mg, 0.90 mmol, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (t, J = 8.8 Hz, 1H), 6.83 (dd, J = 6.8, 2.8 Hz, 1H), 6.64 (ddd, J = 8.8, 4.4, 2.4 Hz, 1H), 6.33 (dd, J = 3.2, 2.0 Hz, 1H), 6.07 (d, J = 3.2 Hz, 1H), 4.76 (s, 2H), 4.59 (s, 1H), 4.07 (d, J = 4.8 Hz, 2H), 3.41 (s, 3H), 3.36 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.9, 152.5, 152.4 (d, *J* = 2.02 Hz), 151.7, 149.4 (d, *J* = 15.15 Hz), 148.0 (d, *J* = 3.03 Hz), 142.7, 124.0, 122.0 (d, *J* = 6.06 Hz), 120.6 (d, *J* = 19.19 Hz), 116.7 (d, *J* = 21.21 Hz), 110.6, 108.8, 70.3, 40.0, 29.4, 28.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -125.6; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{17}ClFN_4O_2^+$: 363.1019; found: 363.1007.



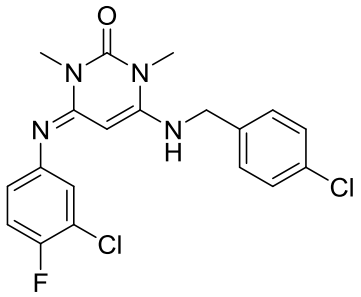
4.1.3.1-2

(E)-4-((3-chloro-4-fluorophenyl)imino)-6-((4-fluorobenzyl)amino)-1,3-dimethyl-3,4-dihydropyrimidin-2(1H)-one (2). Product **2** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (336 mg, 0.86 mmol, 86% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 – 7.11 (m, 2H), 7.07 – 6.94 (m, 3H), 6.78 (dd, J = 6.8, 2.8 Hz, 1H), 6.55 (ddd, J = 8.4, 4.0, 2.4 Hz, 1H), 4.48 (s, 1H), 4.05 (s, 2H), 3.42 (s, 3H), 3.38 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 163.7, 161.2, 154.9, 152.5, 152.2 (d, *J* = 1.01 Hz), 151.7, 149.3, 147.8 (d, *J* = 3.03 Hz), 131.8 (d, *J* = 3.03 Hz), 129.3 (d, *J* = 8.08 Hz), 123.9, 121.7 (d, *J* = 6.06 Hz), 120.7 (d, *J* = 18.18 Hz), 116.7 (d, *J* = 21.21 Hz), 116.0 (d, *J* = 21.21 Hz), 70.9, 46.7, 29.5, 28.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.4, -125.5; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{19}H_{18}ClF_2N_4O^+$: 391.1132; found: 391.1133.



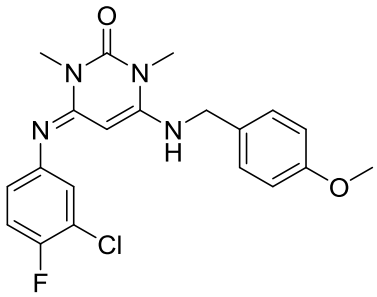
4.1.3.1-3

(E)-4-((3-chloro-4-fluorophenyl)imino)-6-((3-fluorobenzyl)amino)-1,3-dimethyl-3,4-dihydropyrimidin-2(1H)-one (3). Product **3** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (348 mg, 0.89 mmol, 89% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (td, J = 8.0, 6.0 Hz, 1H), 7.08 – 6.85 (m, 4H), 6.76 (dd, J = 6.8, 2.8 Hz, 1H), 6.50 (ddd, J = 8.8, 4.4, 2.4 Hz, 1H), 4.45 (s, 1H), 4.09 (s, 2H), 3.41 (d, J = 5.2 Hz, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 164.3, 161.8, 154.9, 152.5, 152.2 (d, *J* = 1.01 Hz), 151.7, 149.3, 147.7 (d, *J* = 3.03 Hz), 138.7 (d, *J* = 7.07 Hz), 130.6 (d, *J* = 9.09 Hz), 124.0, 123.0 (d, *J* = 3.03 Hz), 121.6 (d, *J* = 7.07 Hz), 120.7 (d, *J* = 18.18 Hz), 116.6 (d, *J* = 21.21 Hz), 115.1 (d, *J* = 21.21 Hz), 114.3 (d, *J* = 22.22 Hz), 71.1, 46.8 (d, *J* = 2.02 Hz), 29.5, 28.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -111.8, -125.5; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{19}H_{18}ClF_2N_4O^+$: 391.1132; found: 391.1137.



4.1.3.1-4

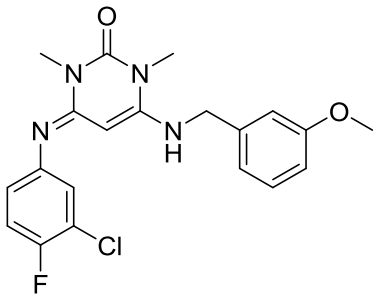
(E)-4-((3-chloro-4-fluorophenyl)imino)-6-((4-chlorobenzyl)amino)-1,3-dimethyl-3,4-dihydropyri midin-2(1H)-one (4). Product **4** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (374 mg, 0.92 mmol, 92% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.29 (m, 2H), 7.15 – 7.06 (m, 2H), 6.99 (t, J = 8.8 Hz, 1H), 6.78 (dd, J = 6.8, 2.4 Hz, 1H), 6.61 – 6.45 (m, 1H), 4.46 (s, 1H), 4.06 (s, 2H), 3.41 (d, J = 14.4 Hz, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 155.0, 152.6, 152.2, 151.6, 149.4, 147.6 (d, J = 4.04 Hz), 134.5, 134.1, 129.0 (d, J = 42.42 Hz), 124.0, 121.7 (d, J = 7.07 Hz), 120.7 (d, J = 19.19 Hz), 116.7 (d, J = 21.21 Hz), 71.0, 46.8, 29.5, 28.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -125.3; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{19}H_{18}Cl_2FN_4O^+$: 407.0836; found: 407.0827.



4.1.3.1-5

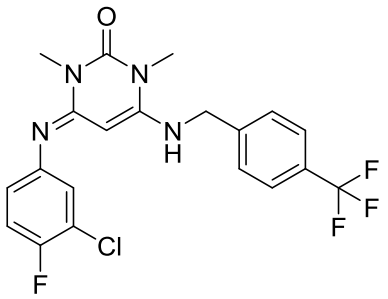
(E)-4-((3-chloro-4-fluorophenyl)imino)-6-((4-methoxybenzyl)amino)-1,3-dimethyl-3,4-dihydropyr imidin-2(1H)-one (5). Product **5** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (342 mg, 0.85 mmol, 85% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (d, J = 7.2 Hz, 2H), 7.00 (td, J = 8.8, 1.6 Hz, 1H), 6.90 – 6.78 (m, 3H), 6.64 – 6.54 (m, 1H), 4.53 (d, J = 1.2 Hz, 1H), 3.99 (s, 2H), 3.81 (d, J = 1.6 Hz, 3H), 3.39 (dd, J = 28.0, 1.6 Hz, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.5, 154.9, 152.5, 152.4 (d, J = 1.01 Hz), 151.7, 149.5, 148.0 (d, J = 3.03 Hz), 129.1, 128.0, 124.0, 121.8 (d, J = 7.07 Hz), 120.7 (d, J = 18.18 Hz), 116.7 (d, J = 21.21 Hz), 114.3, 70.5, 55.3, 46.9, 29.4, 28.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -125.6; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{20}H_{21}ClFN_4O_2^+$: 403.1332; found:

403.1332.



4.1.3.1-6

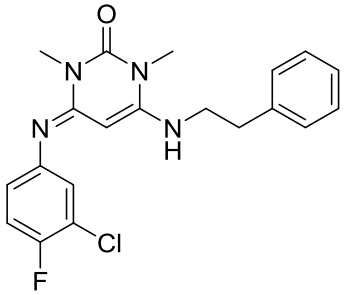
(E)-4-((3-chloro-4-fluorophenyl)imino)-6-((3-methoxybenzyl)amino)-1,3-dimethyl-3,4-dihydropyrimidin-2(1H)-one (6). Product **6** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (358 mg, 0.89 mmol, 89% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.23 (m, 1H), 6.97 (t, *J* = 8.8 Hz, 1H), 6.85 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.80 (dd, *J* = 6.8, 2.4 Hz, 1H), 6.77 – 6.70 (m, 2H), 6.54 (ddd, *J* =8.8, 4.4, 2.4 Hz, 1H), 4.50 (s, 1H), 4.05 (s, 2H), 3.79 (s, 3H), 3.40 (d, *J* = 16.0 Hz, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.0, 154.9, 152.5, 152.4 (d, *J* = 1.01 Hz), 151.7, 149.5, 147.7 (d, *J* = 2.02 Hz), 137.7, 130.1, 124.1, 121.7 (d, *J* = 6.06 Hz), 120.7 (d, *J* = 18.18 Hz), 119.6, 116.6 (d, *J* = 22.22 Hz), 113.3 (d, *J* = 18.18 Hz), 70.8, 55.2, 47.4, 29.5, 28.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -125.6; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{20}H_{21}ClFN_4O_2^+$: 403.1332; found: 403.1340.



4.1.3.1-7

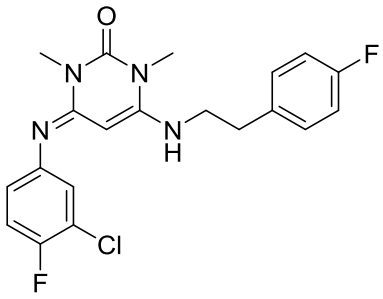
(E)-4-((3-chloro-4-fluorophenyl)imino)-1,3-dimethyl-6-((4-(trifluoromethyl)benzyl)amino)-3,4-dihydropyrimidin-2(1H)-one (7). Product **7** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid

(378 mg, 0.86 mmol, 86% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.0 Hz, 2H), 7.33 – 7.21 (m, 2H), 6.93 (t, *J* = 8.8 Hz, 1H), 6.72 (dd, *J* = 6.8, 2.4 Hz, 1H), 6.46 (ddd, *J* = 8.8, 4.0, 2.4 Hz, 1H), 4.40 (s, 1H), 4.17 (s, 2H), 3.41 (s, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.9, 152.5, 152.0 (d, *J* = 2.02 Hz), 151.6, 149.3, 147.7 (d, *J* = 3.03 Hz), 140.2, 130.4 (d, *J* = 32.32 Hz), 127.6, 126.0 (d, *J* = 4.04 Hz), 123.9, 121.6 (d, *J* = 6.06 Hz), 120.7 (d, *J* = 18.18 Hz), 116.6 (d, *J* = 21.21 Hz), 71.3, 46.8, 29.5, 28.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.6; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{20}H_{18}ClF_4N_4O^+$: 441.1100; found: 441.1106.



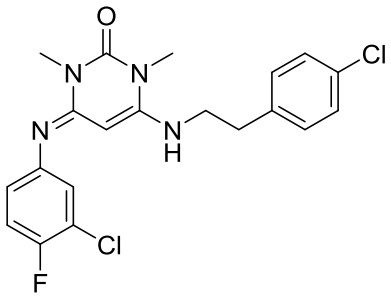
4.1.3.1-8

(E)-4-((3-chloro-4-fluorophenyl)imino)-1,3-dimethyl-6-(phenethylamino)-3,4-dihydropyrimidin-2(1H)-one (8). Product **8** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (351 mg, 0.91 mmol, 91% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.29 (m, 2H), 7.29 – 7.24 (m, 1H), 7.16 – 7.00 (m, 3H), 6.90 (dd, *J* = 6.4, 2.4 Hz, 1H), 6.69 (ddd, *J* = 8.8, 4.4, 2.8 Hz, 1H), 4.53 (s, 1H), 3.44 (s, 3H), 3.21 (s, 3H), 3.19 – 3.09 (m, 2H), 2.84 (t, *J* = 6.8 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.9, 152.5, 152.4 (d, *J* = 1.01 Hz), 151.7, 149.6, 148.1 (d, *J* = 3.03 Hz), 137.5, 128.8 (d, *J* = 50.5 Hz), 127.2, 124.0, 121.8 (d, *J* = 7.07 Hz), 120.8 (d, *J* = 2.02 Hz), 116.8 (d, *J* = 22.22 Hz), 69.6, 43.9, 34.3, 29.4, 28.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -125.6; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{20}H_{21}ClFN_4O^+$: 387.1382; found: 387.1372.



4.1.3.1-9

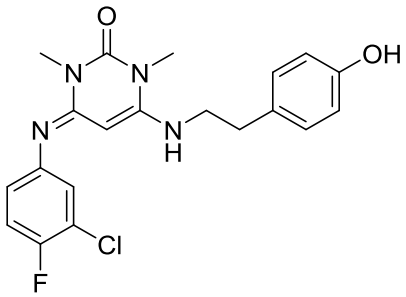
(E)-4-((3-chloro-4-fluorophenyl)imino)-6-((4-fluorophenethyl)amino)-1,3-dimethyl-3,4-dihydropyrimidin-2(1H)-one (9). Product **9** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (364 mg, 0.90 mmol, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 – 6.96 (m, 5H), 6.90 (dd, *J* = 6.8, 2.4 Hz, 1H), 6.73 – 6.64 (m, 1H), 4.52 (s, 1H), 3.43 (s, 3H), 3.24 (s, 3H), 3.13 (s, 2H), 2.81 (t, *J* = 6.8 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 163.1, 160.7, 154.9, 152.5, 152.4 (d, *J* = 1.01 Hz), 151.7,149.5, 148.1 (d, *J* = 3.03 Hz), 133.2 (d, *J* = 3.03 Hz), 130.0 (d, *J* = 8.08 Hz), 124.0, 121.9 (d, *J* = 7.07 Hz), 120.8 (d, *J* = 18.18 Hz), 116.8 (d, *J* = 21.21 Hz), 115.9 (d, *J* = 21.21 Hz) 69.6, 44.0, 33.5, 29.5, 28.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -115.3, -125.5; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{20}H_{20}ClF_2N_4O^+$: 405.1288; found: 405.1296.



4.1.3.1-10

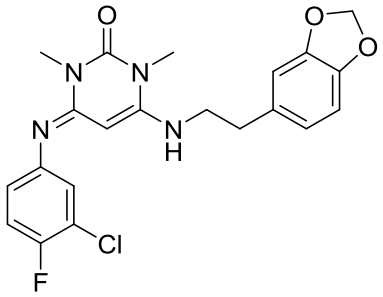
(E)-4-((3-chloro-4-fluorophenyl)imino)-6-((4-chlorophenethyl)amino)-1,3-dimethyl-3,4-dihydropyrimidin-2(1H)-one (10). Product **10** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (386 mg, 0.92 mmol, 92% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.4 Hz, 2H), 7.09 – 6.96 (m, 3H), 6.89 (dd, *J* = 6.8, 2.4 Hz, 1H), 6.73 – 6.64 (m, 1H), 4.51 (s, 1H), 3.43 (s, 3H), 3.24 (s, 3H),

3.13 (s, 2H), 2.80 (t, *J* = 6.8 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 154.9, 152.5, 152.4, 151.7, 149.5, 148.1 (d, *J* = 4.04 Hz) 136.0, 133.0, 129.5 (d, *J* = 74.74 Hz), 124.0, 121.9 (d, *J* = 6.06 Hz), 120.8 (d, *J* = 18.18 Hz), 116.8 (d, *J* = 22.22 Hz), 69.7, 43.9, 33.7, 29.5, 28.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -125.5; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{20}H_{20}Cl_2FN_4O^+$: 421.0993; found: 421.0983.



4.1.3.1-11

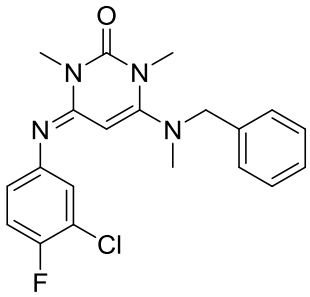
(E)-4-((3-chloro-4-fluorophenyl)imino)-6-((4-hydroxyphenethyl)amino)-1,3-dimethyl-3,4-dihydro pyrimidin-2(1H)-one (11). Product **11** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (354 mg, 0.88 mmol, 88% yield). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.15 (t, *J* = 8.8 Hz, 1H), 6.89 (d, *J* = 6.8 Hz, 1H), 6.83 (d, *J* = 8.0 Hz, 2H), 6.78 – 6.71 (m, 1H), 6.69 (d, *J* = 8.0 Hz, 2H), 4.54 (s, 1H), 3.32 (d, *J* = 10.8 Hz, 6H), 3.12 – 3.04 (m, 2H), 2.71 – 2.61 (m, 2H); $^{13}C\{^{1}H\}$ NMR (101 MHz, Acetone-d_6) δ 156.0, 154.3, 152.7, 151.9, 151.4, 150.6, 149.4 (d, *J* = 3.03 Hz), 129.6, 129.3, 123.8, 122.4 (d, *J* = 7.07 Hz), 119.9 (d, *J* = 19.19 Hz), 116.8 (d, *J* = 21.21 Hz), 115.3, 67.9, 44.8, 33.2, 28.6, 28.2; ^{19}F NMR (376 MHz, Acetone-d_6) δ -127.9; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{20}H_{21}ClFN_4O_2^+$: 403.1332; found:403.1320.



4.1.3.1-12

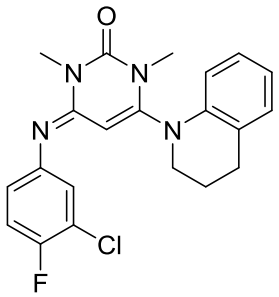
(E)-6-((2-(benzo[d][1,3]dioxol-5-yl)ethyl)amino)-4-((3-chloro-4-fluorophenyl)imino)-1,3-dimethyl-

3,4-dihydropyrimidin-2(1H)-one (12). Product **12** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (383 mg, 0.89 mmol, 89% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (t, *J* = 9.2 Hz, 1H), 6.89 (dd, *J* = 6.8, 2.8 Hz, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 6.72 – 6.66 (m, 1H), 6.59 (d, *J* = 1.6 Hz, 1H), 6.53 (dd, *J* = 7.6, 1.6 Hz, 1H), 5.95 (s, 2H), 4.50 (s, 1H), 3.43 (s, 3H), 3.23 (s, 3H), 3.09 (t, *J* = 6.8 Hz, 2H), 2.76 (t, *J* = 6.8 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 155.0, 152.5, 152.4 (d, *J* = 1.01 Hz), 151.7, 149.6, 148.3, 148.0 (d, *J* = 3.03 Hz), 146.7, 131.1, 124.0, 121.8 (d, *J* = 6.06 Hz), 121.5, 120.8 (d, *J* = 19.19 Hz), 116.8 (d, *J* = 21.21 Hz), 108.6 (d, *J* = 9.09 Hz), 101.2, 69.6, 44.0, 34.0, 29.5, 28.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -125.5; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{21}H_{21}ClFN_4O_3^+$: 431.1281; found:431.1289.



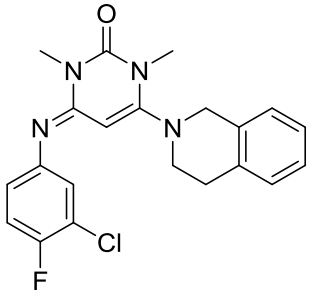
4.1.3.1-13

(E)-6-(benzyl(methyl)amino)-4-((3-chloro-4-fluorophenyl)imino)-1,3-dimethyl-3,4-dihydropyrimidin-2(1H)-one (13). Product **13** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (336 mg, 0.87 mmol, 87% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 3H), 7.23 – 7.14 (m, 2H), 7.03 (t, *J* = 8.8 Hz, 1H), 6.82 (dd, *J* = 6.8, 2.4 Hz, 1H), 6.63 – 6.55 (m, 1H), 4.90 (s, 1H), 3.95 (s, 2H), 3.42 (d, *J* = 5.6 Hz, 6H), 2.51 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 156.1, 155.2, 153.1, 152.7, 151.7 (d, *J* = 1.01 Hz), 147.1 (d, *J* = 3.03 Hz), 135.6, 128.4 (d, *J* = 76.76 Hz), 127.9, 123.8, 121.6 (d, *J* = 6.06 Hz), 120.8 (d, *J* = 19.19 Hz), 116.7 (d, *J* = 21.21 Hz), 82.5, 57.7, 39.9, 32.6, 29.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -124.9; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{20}H_{21}ClFN_4O^+$: 387.1382; found:387.1370.



4.1.3.1-14

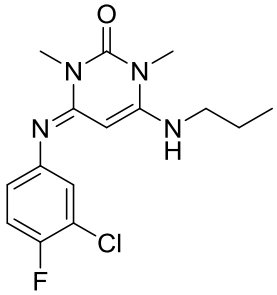
(E)-4-((3-chloro-4-fluorophenyl)imino)-6-(3,4-dihydroquinolin-1(2H)-yl)-1,3-dimethyl-3,4-dihydr opyrimidin-2(1H)-one (14). Product **14** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (354 mg, 0.89 mmol, 89% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 – 6.96 (m, 3H), 6.85 (ddd, *J* = 11.6, 7.2, 1.2 Hz, 2H), 6.64 (ddd, *J* = 8.8, 4.4, 2.8 Hz, 1H), 6.55 (d, *J* = 8.4, 1H), 5.31 (s, 1H), 3.49 (s, 3H), 3.36 (t, *J* = 5.6 Hz, 2H), 3.21 (s, 3H), 2.82 (t, *J* = 6.8 Hz, 2H), 2.09 – 1.93 (m, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 155.3, 152.8 (d, *J* = 7.07 Hz), 152.2, 151.8 (d, *J* = 1.01 Hz), 146.6 (d, *J* = 3.03 Hz), 141.2, 129.8, 127.1, 125.1, 123.6, 121.4 (d, *J* = 7.07 Hz), 121.2, 120.9 (d, *J* = 18.18 Hz), 116.7 (d, *J* = 22.22 Hz), 116.2, 89.4, 49.6, 31.6, 29.6, 26.7, 22.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -124.6; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{21}H_{21}ClFN_4O^+$: 399.1382; found:399.1370.



4.1.3.1-15

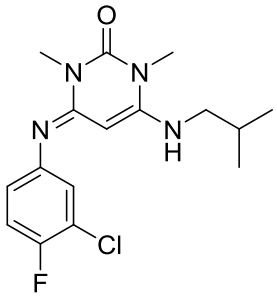
(E)-4-((3-chloro-4-fluorophenyl)imino)-6-(3,4-dihydroisoquinolin-2(1H)-yl)-1,3-dimethyl-3,4-dihy dropyrimidin-2(1H)-one (15). Product **15** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (362 mg, 0.91 mmol, 91% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.11 (m, 3H), 7.09 – 6.98 (m, 2H), 6.87 (dd, *J* = 6.8, 2.4 Hz, 1H), 6.70 – 6.63 (m, 1H), 5.01 (s, 1H), 3.95 (s, 2H), 3.41

(d, *J* = 28.4 Hz, 6H), 3.16 (t, *J* = 5.2 Hz, 2H), 2.96 (t, *J* = 6.0 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 155.9, 155.2, 153.0, 152.8, 151.9 (d, *J* = 1.01 Hz), 147.2 (d, *J* = 4.04 Hz), 133.1, 132.3, 128.9, 127.0, 126.3 (d, *J* = 4.04 Hz), 123.8, 121.4 (d, *J* = 7.07 Hz), 120.9 (d, *J* = 18.18 Hz), 116.8 (d, *J* = 22.22 Hz), 81.4, 52.0, 48.7, 32.4, 29.4, 28.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -124.9; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{21}H_{21}ClFN_4O^+$: 399.1382; found:399.1373.



4.1.3.1-16

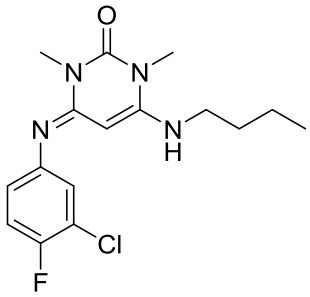
(E)-4-((3-chloro-4-fluorophenyl)imino)-1,3-dimethyl-6-(propylamino)-3,4-dihydropyrimidin-2(1H)-one (16). Product **16** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (301 mg, 0.93 mmol, 93% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (t, *J* = 9.2 Hz, 1H), 6.87 (dd, *J* = 6.8, 2.4 Hz, 1H), 6.68 (ddd, *J* = 8.8, 4.4, 2.8 Hz, 1H), 4.46 (s, 1H), 3.39 (d, *J* = 31.2 Hz, 6H), 2.94 – 2.76 (m, 2H), 1.58 (q, *J* = 7.2 Hz, 2H), 0.93 (t, *J* = 7.6 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 154.8, 152.5 (d, *J* = 1.01 Hz), 152.4, 151.8, 149.8, 148.1 (d, *J* = 3.03 Hz), 124.0, 121.8 (d, *J* = 7.07 Hz), 120.6 (d, *J* = 18.18 Hz), 116.7 (d, *J* = 22.22 Hz), 69.3, 44.7, 29.4, 28.2, 21.8, 11.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -125.8; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{15}H_{19}ClFN_4O^+$: 325.1226; found:325.1232.



4.1.3.1-17

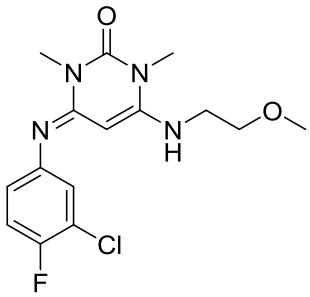
(E)-4-((3-chloro-4-fluorophenyl)imino)-6-(isobutylamino)-1,3-dimethyl-3,4-dihydropyrimidin-2(1

H)-one (17). Product **17** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (304 mg, 0.90 mmol, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (t, *J* = 8.8 Hz, 1H), 6.88 (dd, *J* = 6.8, 2.4 Hz, 1H), 6.68 (ddd, *J* = 8.8, 4.4, 2.4 Hz, 1H), 4.46 (s, 1H), 3.40 (d, *J* = 26.8 Hz, 6H), 2.69 (dd, *J* = 6.8, 4.8 Hz, 2H), 0.93 (d, *J* = 6.4 Hz, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.8, 152.4 (d, *J* = 1.01 Hz),152.4, 151.8, 149.9, 148.0 (d, *J* = 3.03 Hz), 124.0, 121.8 (d, *J* = 7.07 Hz), 120.6 (d, *J* = 19.19 Hz), 116.7 (d, *J* = 21.21 Hz), 69.4, 50.4, 29.5, 28.2, 27.6, 20.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -125.8; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{16}H_{21}ClFN_4O^+$: 339.1382; found:339.1379.



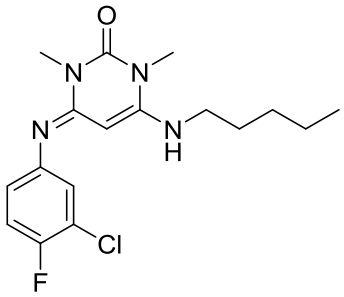
4.1.3.1-18

(E)-6-(butylamino)-4-((3-chloro-4-fluorophenyl)imino)-1,3-dimethyl-3,4-dihydropyrimidin-2(1H) -one (18). Product **18** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (294 mg, 0.87 mmol, 87% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (t, *J* = 8.8 Hz, 1H), 6.88 (dd, *J* = 6.8, 2.4 Hz, 1H), 6.68 (ddd, *J* = 8.8, 4.0, 2.4 Hz, 1H), 4.47 (s, 1H), 3.39 (d, *J* = 34.4 Hz, 6H), 2.87 (td, *J* = 7.2, 4.8 Hz, 2H), 1.60 – 1.48 (m, 2H), 1.37-1.31 (m, 2H), 0.90 (t, *J* = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.8, 152.4 (d, *J* = 1.01 Hz), 152.4, 151.8, 149.8, 148.1 (d, *J* = 3.03 Hz), 124.0, 121.8 (d, *J* = 7.07 Hz), 120.7 (d, *J* = 18.18 Hz), 116.7 (d, *J* = 22.22 Hz), 69.3, 42.7, 30.6, 29.4, 28.2, 20.0, 13.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -125.8; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{16}H_{21}ClFN_4O^+$: 339.1382; found:339.1385.



4.1.3.1-19

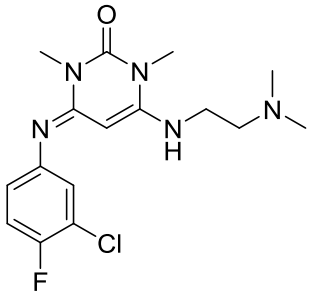
(E)-4-((3-chloro-4-fluorophenyl)imino)-6-((2-methoxyethyl)amino)-1,3-dimethyl-3,4-dihydropyrimidin-2(1H)-one (19). Product **19** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (286 mg, 0.84 mmol, 84% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (t, *J* = 8.8 Hz, 1H), 6.87 (dd, *J* = 6.8, 2.4 Hz, 1H), 6.70 – 6.65 (m, 1H), 4.46 (s, 1H), 3.55 – 3.52 (m, 2H), 3.44 (s, 3H), 3.36 (s, 3H), 3.02 (q, *J* = 4.8 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.8, 152.4 (d, *J* = 3.03 Hz), 151.7, 150.0, 148.0 (d, *J* = 3.03 Hz), 124.0, 121.8 (d, *J* = 6.06 Hz), 120.7 (d, *J* = 18.18 Hz), 116.7 (d, *J* = 22.22 Hz), 69.6, 69.2, 58.9, 42.4, 29.5, 28.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -125.8; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{15}H_{19}ClFN_4O_2^+$: 341.1175; found:341.1173.



4.1.3.1-20

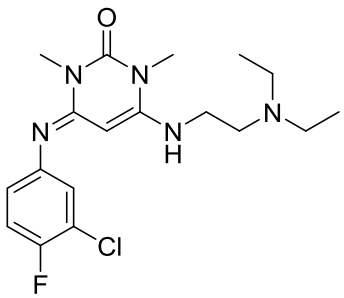
(E)-4-((3-chloro-4-fluorophenyl)imino)-1,3-dimethyl-6-(pentylamino)-3,4-dihydropyrimidin-2(1H)-one (20). Product **20** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (310 mg, 0.88 mmol, 88% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 (t, *J* = 8.8 Hz, 1H), 6.87 (dd, *J* = 6.8, 2.4 Hz, 1H), 6.67 (ddd, *J* = 8.8, 4.4, 2.4 Hz, 1H), 4.45 (s, 1H), 3.42 (s, 3H), 3.34 (s, 3H), 2.86 (q, *J* = 7.2 Hz, 2H), 1.61 – 1.46 (m, 2H), 1.32 – 1.23 (m, 4H), 0.87 (t, *J* = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz,

$CDCl_3$) δ 154.8, 152.5 (d, *J* = 1.01 Hz), 152.4, 151.8, 149.8, 148.1 (d, *J* = 3.03 Hz), 124.0, 121.8 (d, *J* = 6.06 Hz), 120.7 (d, *J* = 18.18 Hz), 116.7 (d, *J* = 21.21 Hz), 69.3, 43.0, 29.4, 29.0, 28.2, 28.2, 22.3, 13.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -125.8; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{23}ClFN_4O^+$: 353.1539; found:353.1534.



4.1.3.1-21

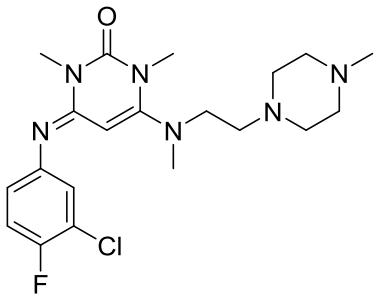
(E)-4-((3-chloro-4-fluorophenyl)imino)-6-((2-(dimethylamino)ethyl)amino)-1,3-dimethyl-3,4-dihydropyrimidin-2(1H)-one (21). Product **21** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (318 mg, 0.90 mmol, 90% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 7.03 (t, *J* = 8.8 Hz, 1H), 6.88 (dd, *J* = 6.4, 2.4Hz, 1H), 6.69 (ddd, *J* = 8.8, 4.4, 2.8 Hz, 1H), 4.41 (s, 1H), 3.40 (d, *J* = 38.4 Hz, 6H), 2.86 (t, *J* = 5.6 Hz, 2H), 2.50 (dd, *J* = 6.4, 4.8 Hz, 2H), 2.22 (s, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 154.8, 152.6 (d, *J* = 1.01 Hz), 152.4, 151.8, 150.1, 148.2 (d, *J* = 3.03 Hz), 124.0, 121.8 (d, *J* = 7.07 Hz), 120.7 (d, *J* = 18.18 Hz), 116.7 (d, *J* = 21.21 Hz), 69.1, 56.2, 44.8, 39.5, 29.4, 28.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -125.9; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{16}H_{22}ClFN_5O^+$: 354.1491; found:354.1480.



4.1.3.1-22

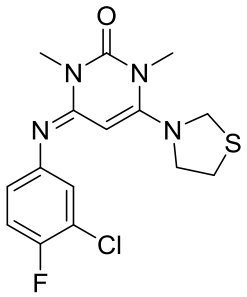
(E)-4-((3-chloro-4-fluorophenyl)imino)-6-((2-(diethylamino)ethyl)amino)-1,3-dimethyl-3,4-dihydr

opyrimidin-2(1H)-one (22). Product **22** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (335 mg, 0.88 mmol, 88% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 (t, *J* = 8.8 Hz, 1H), 6.87 (dd, *J* = 6.4, 2.4 Hz, 1H), 6.67 (ddd, *J* = 8.4, 4.0, 2.4 Hz, 1H), 4.39 (s, 1H), 3.38 (d, *J* = 42.8 Hz, 6H), 2.82 (t, *J* = 5.6 Hz, 2H), 2.63 (t, *J* = 5.6 Hz, 2H), 2.49 (q, *J* = 7.2 Hz, 4H), 0.99 (t, *J* = 6.8 Hz, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.8, 152.7 (d, *J* = 1.01 Hz), 152.4, 151.8, 150.0, 148.3 (d, *J* = 3.03 Hz), 124.0, 121.9 (d, *J* = 7.07 Hz), 120.6 (d, *J* = 18.18 Hz), 116.7 (d, *J* = 21.21 Hz), 69.0, 49.8, 46.3, 39.3, 29.4, 28.3, 12.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -126.0; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{18}H_{26}ClFN_5O^+$: 382.1804; found:382.1791.



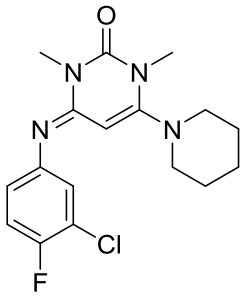
4.1.3.1-23

(E)-4-((3-chloro-4-fluorophenyl)imino)-1,3-dimethyl-6-(methyl(2-(4-methylpiperazin-1-yl)ethyl)amino)-3,4-dihydropyrimidin-2(1H)-one (23). Product **23** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (methylene chloride: methanol = 20 : 1). yellow liquid (363 mg, 0.86 mmol, 86% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (t, *J* = 8.8 Hz, 1H), 6.84 (dd, *J* = 6.8, 2.4 Hz, 1H), 6.64 (ddd, *J* = 8.8, 4.4, 2.8 Hz, 1H), 4.88 (s, 1H), 3.41 (s, 3H), 3.30 (s, 3H), 2.81 (t, *J* = 6.0 Hz, 5H), 2.77 – 2.70 (m, 1H) , 2.60 (s,8H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 156.0, 155.2, 153.0, 152.8, 151.8, 147.1 (d, *J* = 4.04 Hz), 123.7, 121.5 (d, *J* = 6.06 Hz), 120.9 (d, *J* = 18.18 Hz), 116.8 (d, *J* = 21.21 Hz), 81.4, 55.2, 54.1, 52.5, 50.0, 44.6, 32.1, 29.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -124.9; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{20}H_{29}ClFN_6O^+$: 423.2070; found:423.2073.



4.1.3.1-24

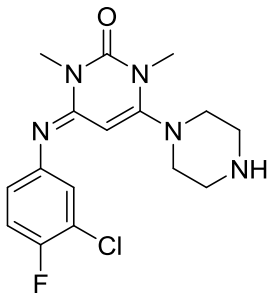
(E)-4-((3-chloro-4-fluorophenyl)imino)-1,3-dimethyl-6-(thiazolidin-3-yl)-3,4-dihydropyrimidin-2(1H)-one (24). Product **24** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (315 mg, 0.89 mmol, 89% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (t, *J* = 8.8 Hz, 1H), 6.85 (dd, *J* = 6.8, 2.8 Hz, 1H), 6.64 (ddd, *J* = 8.8, 4.0, 2.4 Hz, 1H), 5.24 (s, 1H), 4.19 (s, 2H), 3.41 (d, *J* = 7.2 Hz, 6H), 3.34 (t, *J* = 6.0 Hz, 2H), 2.91 (t, *J* = 6.4 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 155.2, 153.2, 152.8 (d, *J* = 10.1 Hz), 151.4 (d, *J* = 2.02 Hz), 146.8 (d, *J* = 3.03 Hz), 123.7, 121.4 (d, *J* = 7.07 Hz), 120.9 (d, *J* = 18.18 Hz), 116.8 (d, *J* = 22.22 Hz), 81.6, 55.0, 54.5, 32.6, 30.0, 29.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -124.6; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{15}H_{17}ClFN_4OS^+$: 355.0790; found:355.0780.



4.1.3.1-25

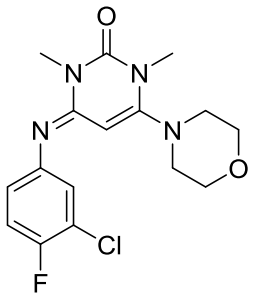
(E)-4-((3-chloro-4-fluorophenyl)imino)-1,3-dimethyl-6-(piperidin-1-yl)-3,4-dihydropyrimidin-2(1H)-one (25). Product **25** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (319 mg, 0.91 mmol, 91% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (t, *J* = 8.8 Hz, 1H), 6.86 (dd, *J* = 6.4, 2.4 Hz, 1H), 6.66 (ddd, *J* = 8.8, 4.4, 2.8 Hz, 1H), 4.86 (s, 1H), 3.42 (s, 3H), 3.31 (s, 3H), 2.71 (s, 4H), 1.72 – 1.50 (m, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 157.1, 155.1, 153.1, 152.7, 152.2 (d, *J* = 1.01 Hz),

147.3 (d, *J* = 3.03 Hz), 123.8, 121.5 (d, *J* = 6.06 Hz), 120.8 (d, *J* = 18.18 Hz), 116.7 (d, *J* = 22.22 Hz), 81.0, 51.5, 32.1, 29.3, 25.3, 23.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -125.1; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{21}ClFN_4O^+$: 351.1382; found:351.1377.



4.1.3.1-26

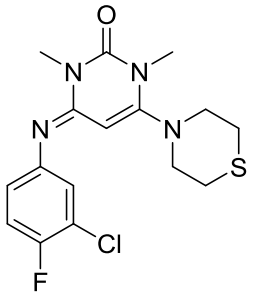
(E)-4-((3-chloro-4-fluorophenyl)imino)-1,3-dimethyl-6-(piperazin-1-yl)-3,4-dihydropyrimidin-2(1H)-one (26). Product **26** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (305 mg, 0.87 mmol, 87% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 (t, *J* = 8.8 Hz, 1H), 6.83 (dd, *J* = 6.4, 2.4 Hz, 1H), 6.63 (ddd, *J* = 8.8, 4.0, 2.4 Hz, 1H), 4.87 (s, 1H), 3.39 (s, 3H), 3.30 (s, 3H), 3.13 (s, H), 2.93 (t, *J* = 4.8 Hz, 4H), 2.74 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 156.3, 155.1, 153.0, 152.7, 151.9 (d, *J* = 1.01 Hz), 147.1 (d, *J* = 3.03 Hz), 123.7, 121.4 (d, *J* = 7.07 Hz), 120.8 (d, *J* = 18.18 Hz), 116.8 (d, *J* = 21.21 Hz), 81.3, 51.2, 45.1, 32.1, 29.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -124.9; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{16}H_{20}ClFN_5O^+$: 352.1335; found:352.1326.



4.1.3.1-27

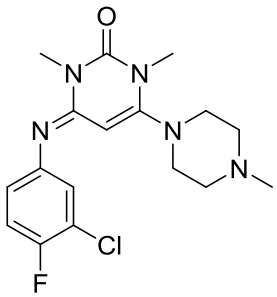
(E)-4-((3-chloro-4-fluorophenyl)imino)-1,3-dimethyl-6-morpholino-3,4-dihydropyrimidin-2(1H)-one (27). Product **27** was synthesized according to general experimental procedure Ⅲ and purified by

column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (313 mg, 0.89 mmol, 89% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (t, *J* = 8.8 Hz, 1H), 6.85 (dd, *J* = 6.4, 2.4 Hz, 1H), 6.65 (ddd, *J* = 8.8, 4.0, 2.4 Hz, 1H), 4.90 (s, 1H), 3.75 (t, *J* = 4.8 Hz, 4H), 3.41 (s, 3H), 3.33 (s, 3H), 2.77 (t, *J* = 4.8 Hz, 4H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 155.9, 155.2, 152.8 (d, *J* = 13.13 Hz), 151.7 (d, *J* = 1.01 Hz), 147.0 (d, *J* = 4.04 Hz), 123.7, 121.4 (d, *J* = 7.07 Hz), 120.9 (d, *J* = 18.18 Hz), 116.8 (d, *J* = 22.22 Hz), 81.4, 66.1, 50.6, 32.1, 29.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -124.7; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{16}H_{19}ClFN_4O_2^+$: 353.1175; found:353.1162.



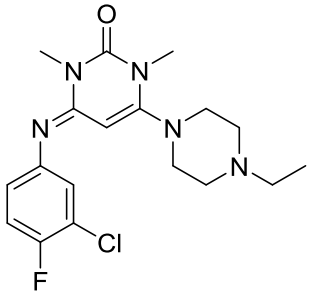
4.1.3.1-28

(E)-4-((3-chloro-4-fluorophenyl)imino)-1,3-dimethyl-6-thiomorpholino-3,4-dihydropyrimidin-2(1H)-one (28). Product **28** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (305 mg, 0.83 mmol, 83% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (t, *J* = 8.8 Hz, 1H), 6.85 (dd, *J* = 6.4, 2.4 Hz, 1H), 6.70 – 6.57 (m, 1H), 4.91 (s, 1H), 3.42 (s, 3H), 3.31 (s, 3H), 3.02 (s, 4H), 2.71 (s, 4H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 156.7, 155.2, 152.8 (d, *J* = 3.03 Hz), 151.7, 147.0 (d, *J* = 4.04 Hz), 123.7, 121.3 (d, *J* = 6.06 Hz), 121.0 (d, *J* = 18.18 Hz), 116.8 (d, *J* = 21.21 Hz), 82.4, 52.7, 31.9, 29.4, 27.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -124.7; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{16}H_{19}ClFN_4OS^+$: 369.0947; found:369.0942.



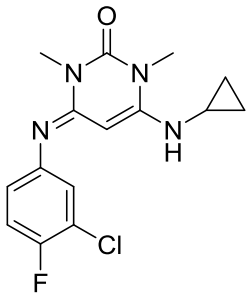
4.1.3.1-29

(E)-4-((3-chloro-4-fluorophenyl)imino)-1,3-dimethyl-6-(4-methylpiperazin-1-yl)-3,4-dihydropyrimidin-2(1H)-one (29). Product **29** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (321 mg, 0.88 mmol, 88% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (t, *J* = 8.8 Hz, 1H), 6.85 (dd, *J* = 6.8, 2.8 Hz, 1H), 6.73 – 6.59 (m, 1H), 4.91 (s, 1H), 3.41 (s, 3H), 3.31 (s, 3H), 2.79 (s, 4H), 2.47 (s, 4H), 2.30 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 156.2, 155.2, 152.9 (d, *J* = 26.26 Hz), 151.9, 147.1 (d, *J* = 3.03 Hz), 123.7, 121.4 (d, *J* = 7.07 Hz), 120.9 (d, *J* = 19.19 Hz), 116.8 (d, *J* = 21.21 Hz), 81.2, 54.2, 50.1, 46.0, 32.2, 29.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -124.9; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{22}ClFN_5O^+$: 366.1491; found:366.1480.



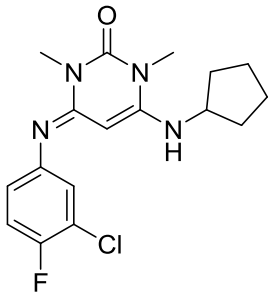
4.1.3.1-30

(E)-4-((3-chloro-4-fluorophenyl)imino)-6-(4-ethylpiperazin-1-yl)-1,3-dimethyl-3,4-dihydropyrimidin-2(1H)-one (30). Product **30** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (326 mg, 0.86 mmol, 86% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (t, *J* = 8.8 Hz, 1H), 6.84 (dd, *J* = 6.4, 2.4 Hz, 1H), 6.64 (ddd, *J* = 8.4, 4.0, 2.4 Hz, 1H), 4.91 (s, 1H), 3.41 (s, 3H), 3.31 (s, 3H), 2.80 (s, 4H), 2.51 (s, 3H), 2.42 (q, *J* = 7.2 Hz, 3H), 1.06 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 156.2, 155.2, 152.9 (d, *J* = 25.25 Hz) 151.9 (d, *J* = 1.01 Hz), 147.1 (d, *J* = 3.03 Hz), 123.7, 121.4 (d, *J* = 7.07 Hz), 120.9 (d, *J* = 19.19 Hz), 116.8 (d, *J* = 21.21 Hz), 81.3, 52.1, 52.0, 50.2, 32.1, 29.4, 12.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -124.9; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{18}H_{24}ClFN_5O^+$: 380.1684; found:380.1636.



4.1.3.1-31

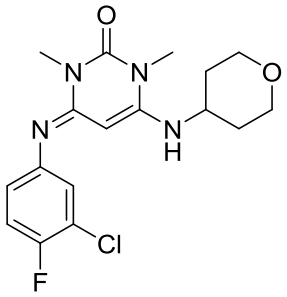
(E)-4-((3-chloro-4-fluorophenyl)imino)-6-(cyclopropylamino)-1,3-dimethyl-3,4-dihydropyrimidin-2(1H)-one (31). Product **31** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (293 mg, 0.91 mmol, 91% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (t, *J* = 8.8Hz, 1H), 6.93 (dd, *J* = 6.8, 2.4 Hz, 1H), 6.73 (ddd, *J* = 8.8, 4.4, 2.8 Hz, 1H), 4.98 (s, 1H), 3.44 (s, 3H), 3.29 (s, 3H), 2.32 – 2.17 (m, 1H), 0.75 – 0.62 (m, 2H), 0.57 – 0.45 (m, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.8, 152.6 (d, *J* = 1.01 Hz), 152.4, 151.8, 150.6, 148.0 (d, *J* = 3.03 Hz), 124.1, 122.0 (d, *J* = 7.07 Hz), 120.5 (d, *J* = 18.18 Hz), 116.6 (d, *J* = 21.21 Hz), 71.3, 29.5, 28.3, 24.3, 7.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -125.7; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{15}H_{17}ClFN_4O^+$: 323.1069; found:323.1060.



4.1.3.1-32

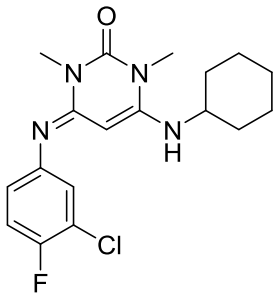
(E)-4-((3-chloro-4-fluorophenyl)imino)-6-(cyclopentylamino)-1,3-dimethyl-3,4-dihydropyrimidin-2(1H)-one (32). Product **32** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (311 mg, 0.89 mmol, 89% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 (t, *J* = 8.4 Hz, 1H), 6.88 (dd, *J* = 6.8,2.8 Hz, 1H), 6.76 – 6.62 (m, 1H), 4.51 (s, 1H), 3.92 (s, 1H), 3.43 (s, 3H), 3.33 (s, 3H), 1.93 – 1.82 (m, 2H), 1.73 – 1.53 (m, 4H), 1.48-1.36 (m, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.8, 152.5 (d, *J*

= 1.01 Hz), 152.4, 151.8, 149.3, 148.0 (d, *J* = 3.03 Hz), 124.1, 122.0 (d, *J* = 6.06 Hz), 120.6 (d, *J* = 18.18 Hz), 116.6 (d, *J* = 21.21 Hz), 70.5, 54.0, 33.2, 29.4, 28.3, 24.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -125.8; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{21}ClFN_4O^+$: 351.1382; found:351.1378.



4.1.3.1-33

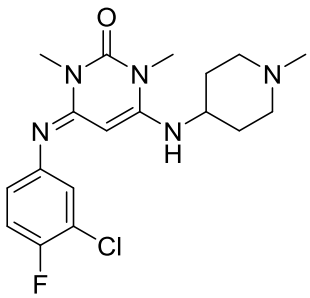
(E)-4-((3-chloro-4-fluorophenyl)imino)-1,3-dimethyl-6-((tetrahydro-2H-pyran-4-yl)amino)-3,4-dihydropyrimidin-2(1H)-one (33). Product **33** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (299 mg, 0.85 mmol, 85% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (t, *J* = 8.8 Hz, 1H), 6.87 (dd, *J* = 6.4, 2.4 Hz, 1H), 6.68 (ddd, *J* = 8.8, 4.4, 2.4 Hz, 1H), 4.53 (s, 1H), 3.92 (dt, *J* = 12.0, 3.6 Hz, 2H), 3.43 (s, 3H), 3.35 (s, 3H), 3.18 (s, 1H), 1.89 (d, *J* = 12.4 Hz, 2H), 1.55 – 1.42 (m, 2H), 1.27 – 1.19 (m, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.8, 152.4, 152.3 (d, *J* = 1.01 Hz), 151.8, 148.4, 147.8 (d, *J* = 3.03 Hz), 124.0, 121.9 (d, *J* = 6.06 Hz), 120.6 (d, *J* = 18.18 Hz), 116.6 (d, *J* = 21.21 Hz), 70.0, 66.1, 48.8, 32.6, 29.5, 28.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -125.4; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{21}ClFN_4O_2^+$: 367.1332; found:367.1319.



4.1.3.1-34

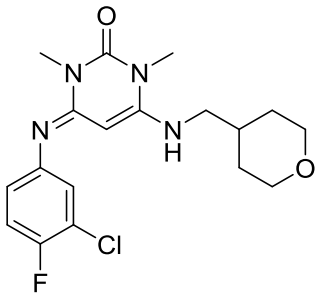
(E)-4-((3-chloro-4-fluorophenyl)imino)-6-(cyclohexylamino)-1,3-dimethyl-3,4-dihydropyrimidin-2(1H)-one (34). Product **34** was synthesized according to general experimental procedure Ⅲ and

purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (335 mg, 0.92 mmol, 92% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (t, *J* = 9.2 Hz, 1H), 6.90 (dd, *J* = 6.8, 2.8 Hz, 1H), 6.76 – 6.63 (m, 1H), 4.52 (s, 1H), 3.85 (d, *J* = 6.8 Hz, 1H), 3.44 (s, 3H), 3.34 (s, 3H), 3.03 – 2.89 (m, 1H), 1.90 (d, *J* = 11.2 Hz, 2H), 1.76 – 1.65 (m, 2H), 1.60 (d, *J* = 9.6 Hz, 1H), 1.30 – 1.13 (m, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.8, 152.6 (d, *J* = 1.01 Hz), 152.4, 151.9, 148.6, 148.1 (d, *J* = 3.03 Hz), 124.1, 122.0 (d, *J* = 6.06 Hz), 120.5 (d, *J* = 18.18 Hz), 116.6 (d, *J* = 22.22 Hz), 69.6, 51.3, 32.4, 29.4, 28.2, 25.4, 24.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -125.8; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{18}H_{23}ClFN_4O^+$: 365.1539; found:365.1527.



4.1.3.1-35

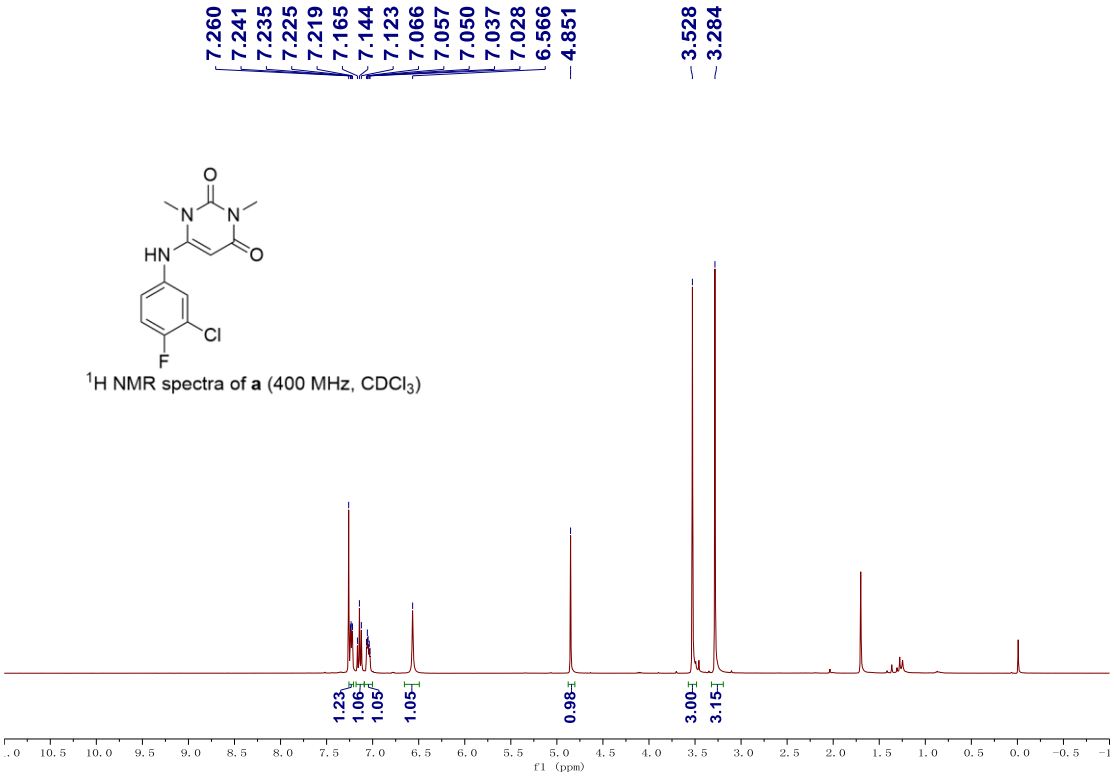
(E)-4-((3-chloro-4-fluorophenyl)imino)-1,3-dimethyl-6-((1-methylpiperidin-4-yl)amino)-3,4-dihydropyrimidin-2(1H)-one (35). Product **35** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (methylene chloride: methanol= 20 : 1). yellow liquid (307 mg, 0.81 mmol, 81% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (t, *J* = 8.8 Hz, 1H), 6.89 (dd, *J* = 6.8, 2.4 Hz, 1H), 6.69 (ddd, *J* = 8.8, 4.4, 2.8 Hz, 1H), 4.52 (s, 1H), 3.44 (s, 3H), 3.36 (s, 3H), 3.04 – 2.90 (m, 1H), 2.74 (d, *J* = 11.2 Hz, 2H), 2.28 (s, 3H), 2.18 – 1.99 (m, 3H), 1.93 (d, *J* = 12.8 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.8, 152.4, 151.8, 148.6, 148.0 (d, *J* = 3.03 Hz), 124.0, 121.9 (d, *J* = 6.06 Hz), 120.6 (d, *J* = 18.18 Hz), 116.6 (d, *J* = 21.21 Hz), 69.9, 53.7, 46.0, 31.7, 29.4, 28.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -125.7; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{18}H_{24}ClFN_5O^+$: 380.1648; found:380.1651.



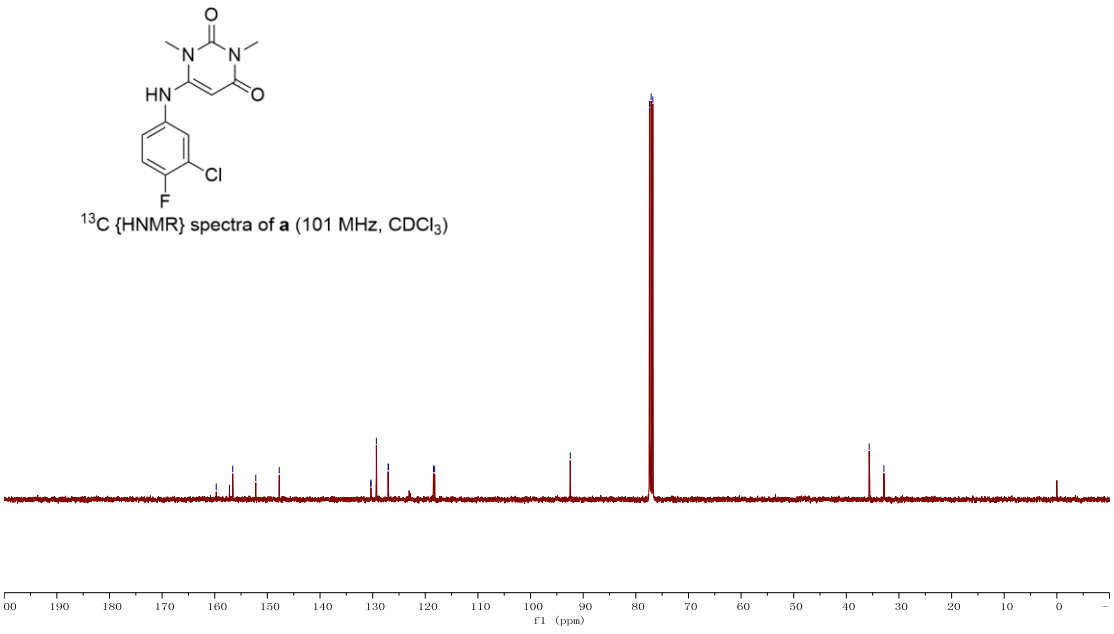
4.1.3.1-36

(E)-4-((3-chloro-4-fluorophenyl)imino)-1,3-dimethyl-6-(((tetrahydro-2H-pyran-4-yl)methyl)amino)-3,4-dihydropyrimidin-2(1H)-one (36). Product **36** was synthesized according to general experimental procedure Ⅲ and purified by column chromatography (petroleum ether : ethyl acetate= 20 : 1-1 : 5). yellow liquid (319 mg, 0.84 mmol, 84% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (t, *J* = 8.8 Hz, 1H), 6.87 (dd, *J* = 6.8, 2.4 Hz, 1H), 6.68 (ddd, *J* = 8.4, 4.0, 2.4 Hz, 1H), 4.45 (s, 1H), 3.96 (dd, *J* = 11.2, 3.2 Hz, 4H), 3.46 – 3.29 (m, 8H), 2.79 (d, *J* = 6.4 Hz, 2H), 1.82 – 1.70 (m, 1H), 1.58 – 1.49 (m, 2H), 1.32 – 1.25 (m, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.8, 152.4, 152.4 (d, *J* = 1.01 Hz), 151.7, 149.8, 148.0 (d, *J* = 4.04 Hz), 123.9, 121.9 (d, *J* = 7.07 Hz), 120.6 (d, *J* = 19.19 Hz), 116.7 (d, *J* = 21.21 Hz), 69.6, 67.4, 48.8, 34.2, 30.8, 29.5, 28.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -125.5; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{18}H_{23}ClFN_4O_2^+$: 381.1488; found:381.1484.

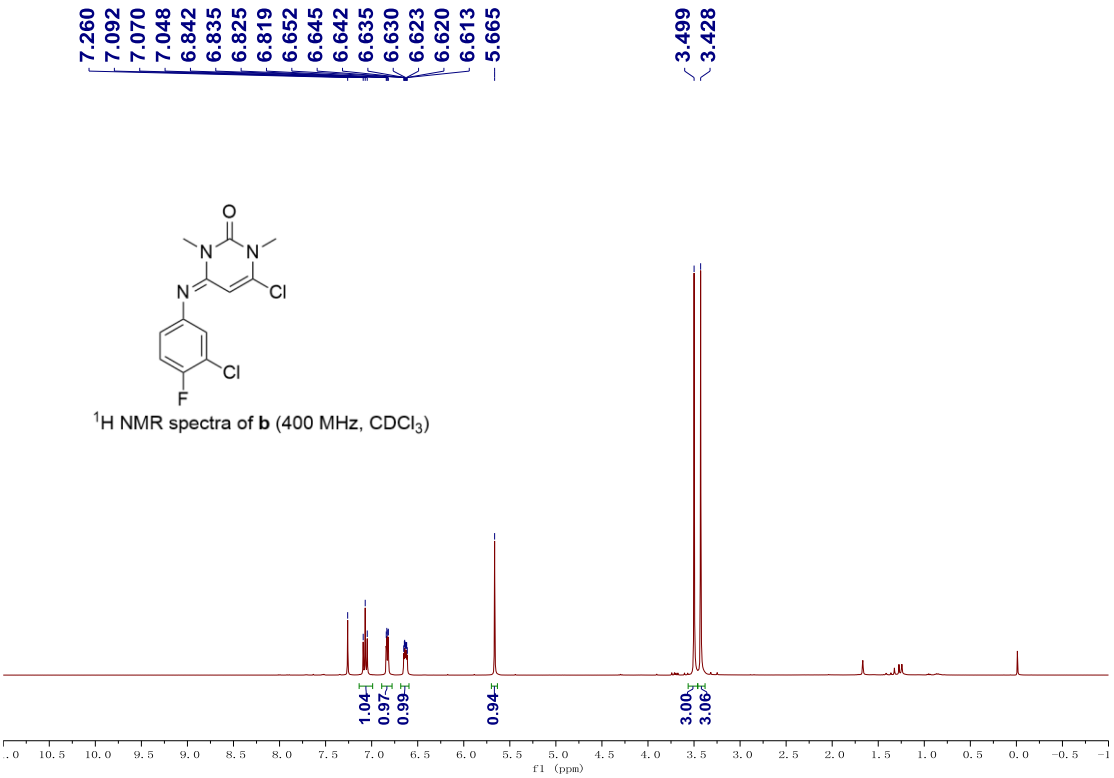
4. ^{1}H NMR, ^{13}C NMR spectra and HRMS



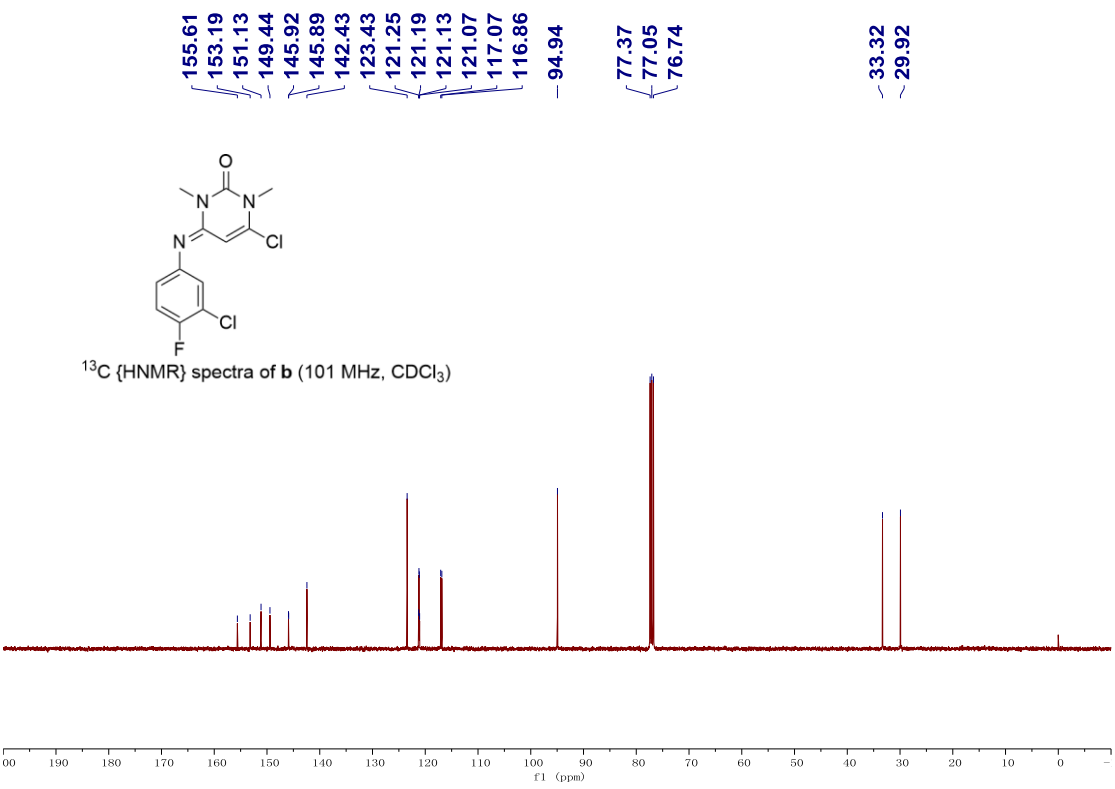
^{1}H NMR spectra of **a** (400 MHz, $CDCl_3$)



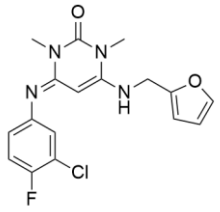
^{13}C {HNMR} spectra of **a** (101 MHz, $CDCl_3$)



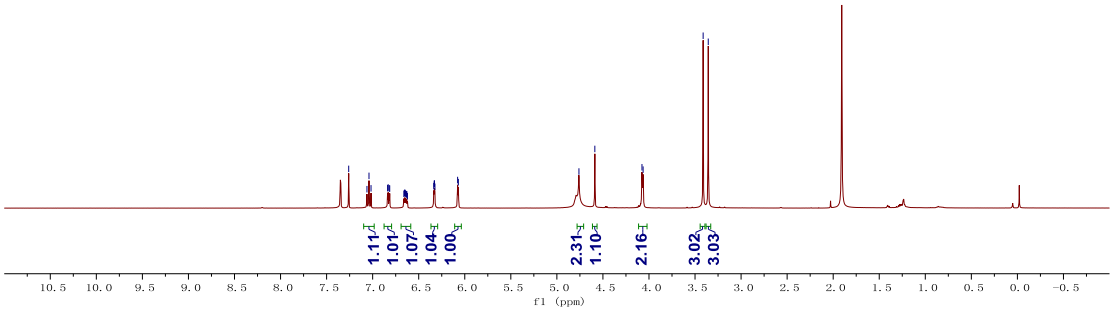
^{1}H NMR spectra of **b** (400 MHz, $CDCl_3$)

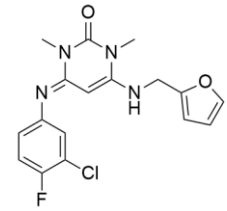


^{13}C {HNMR} spectra of **b** (101 MHz, $CDCl_3$)

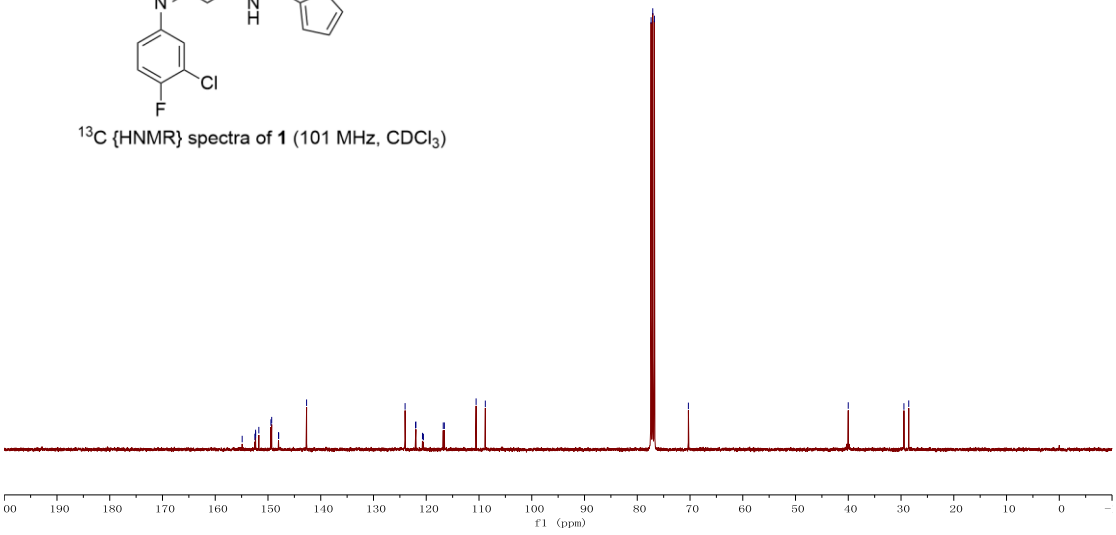


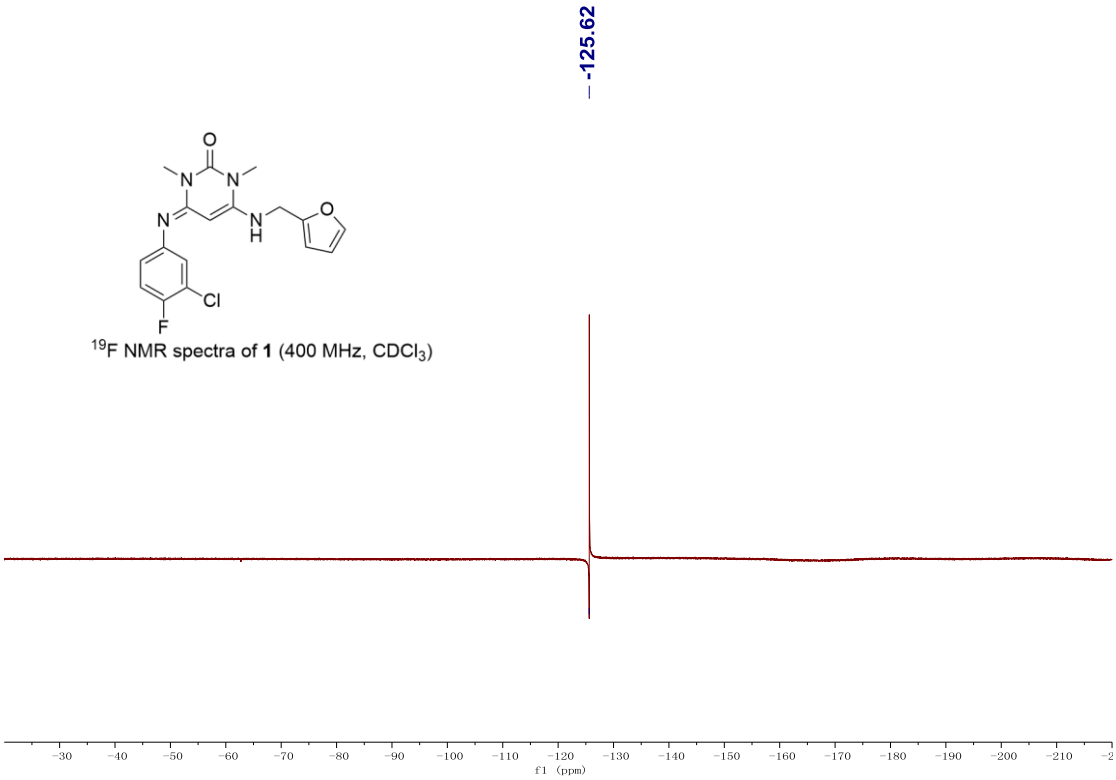
^{1}H NMR spectra of **1** (400 MHz, $CDCl_3$)



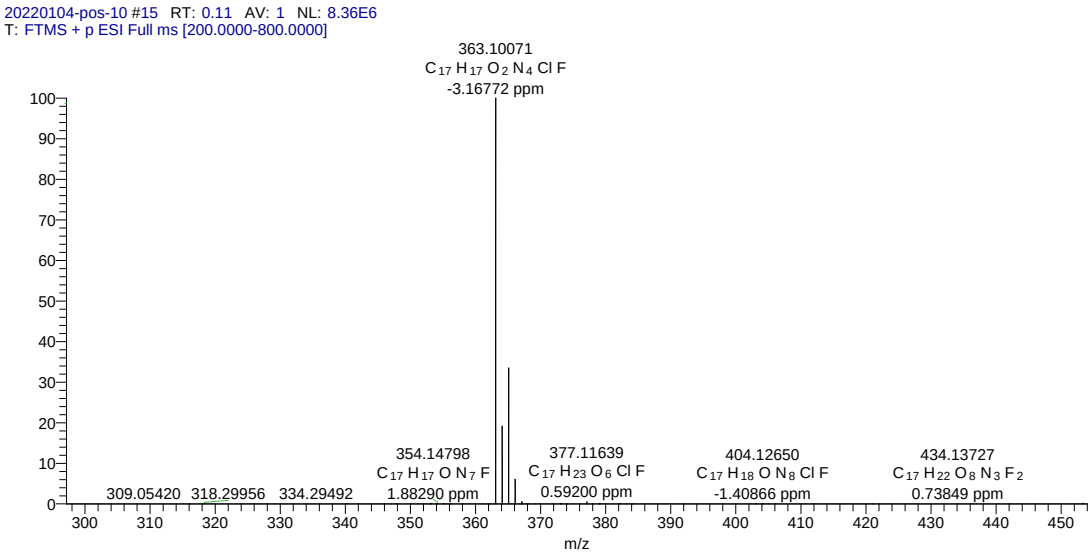


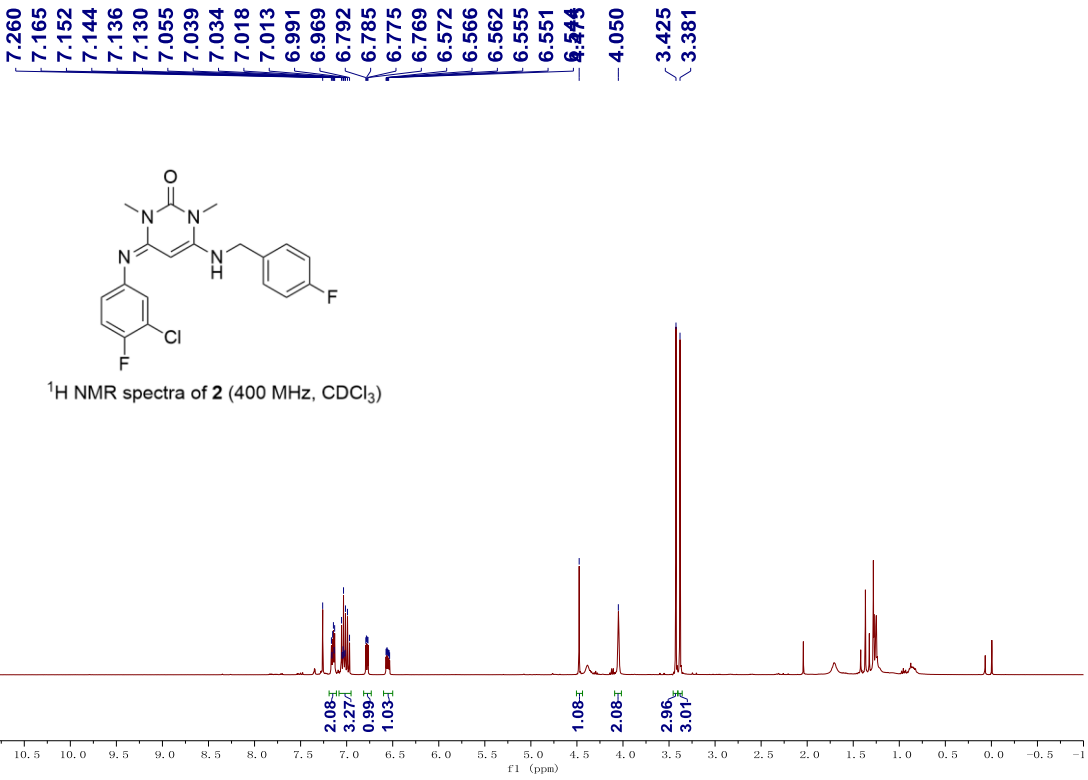
^{13}C {HNMR} spectra of **1** (101 MHz, $CDCl_3$)



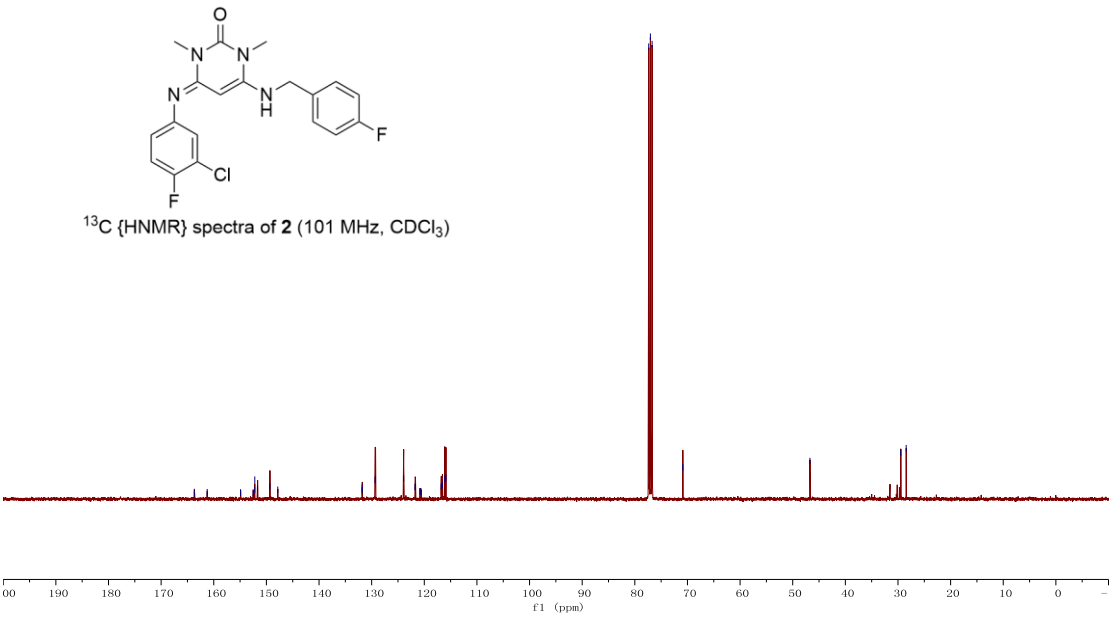


^{19}F NMR spectra of **1** (400 MHz, $CDCl_3$)

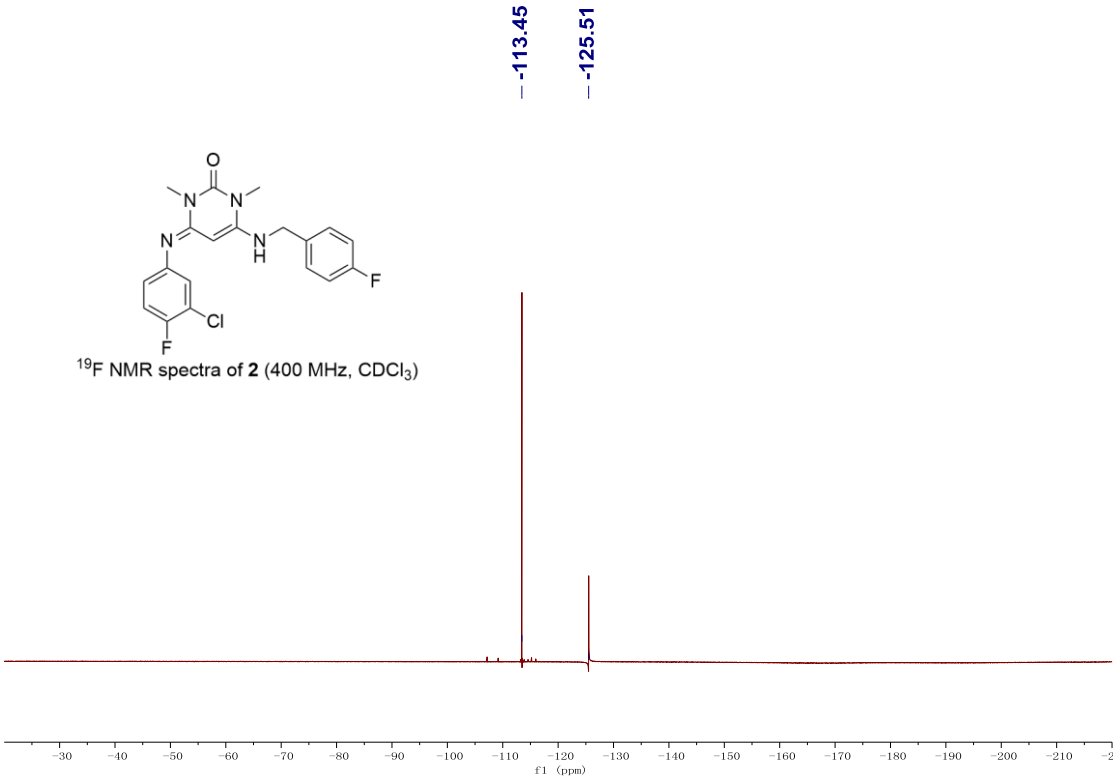




^{1}H NMR spectra of **2** (400 MHz, $CDCl_3$)



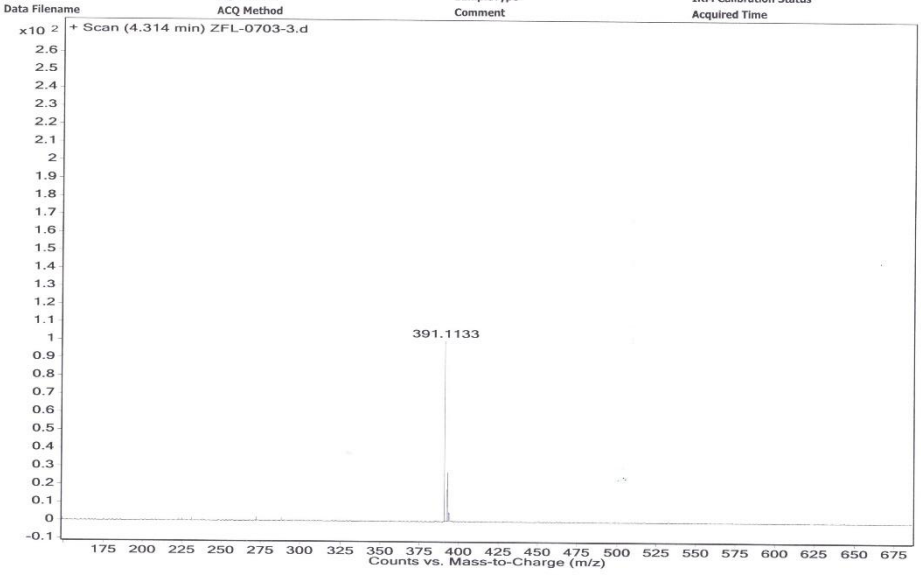
^{13}C {HNMR} spectra of **2** (101 MHz, $CDCl_3$)

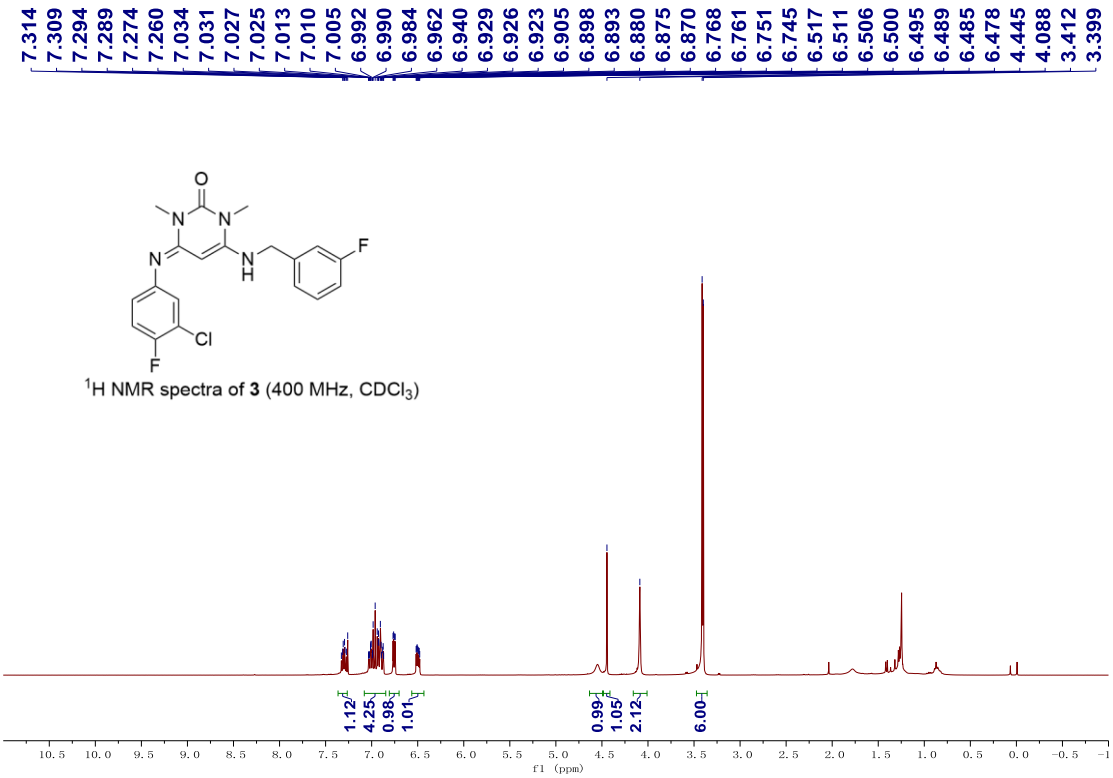


^{19}F NMR spectra of **2** (400 MHz, $CDCl_3$)

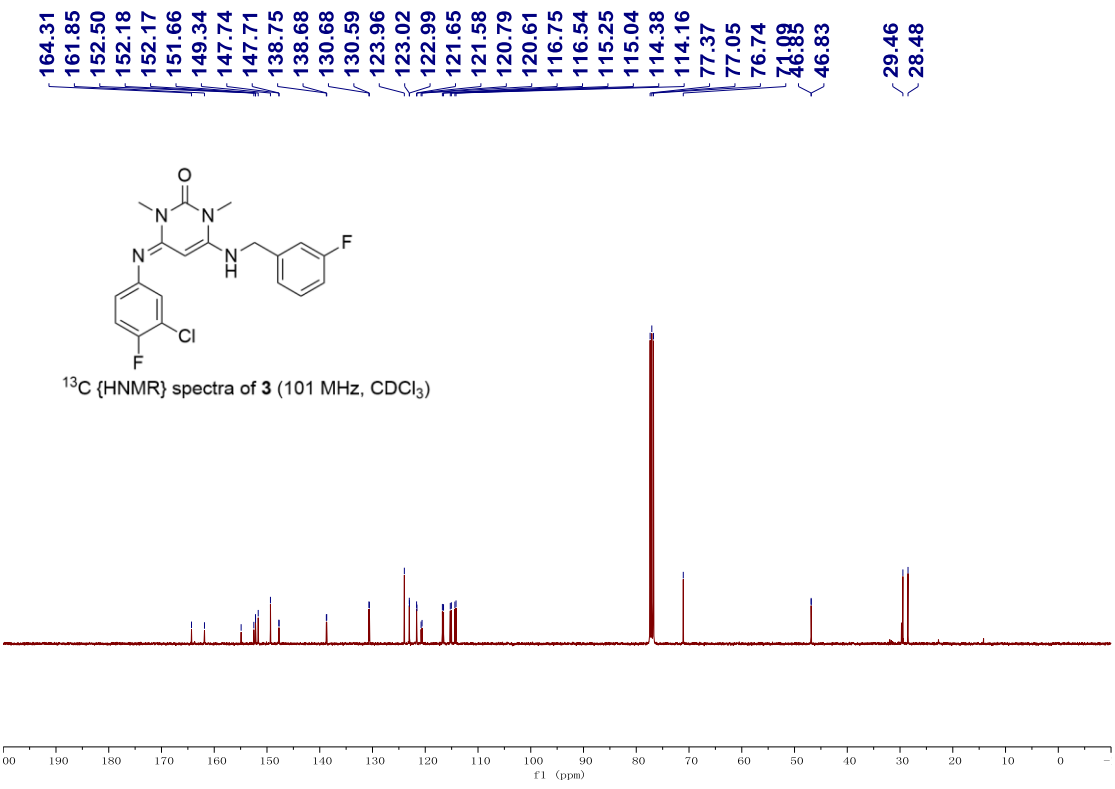
6.

Sample Name	Position	Instrument Name	User Name
Inj Vol	InjPosition	SampleType	IRM Calibration Status
Data Filename	ACQ Method	Comment	Acquired Time

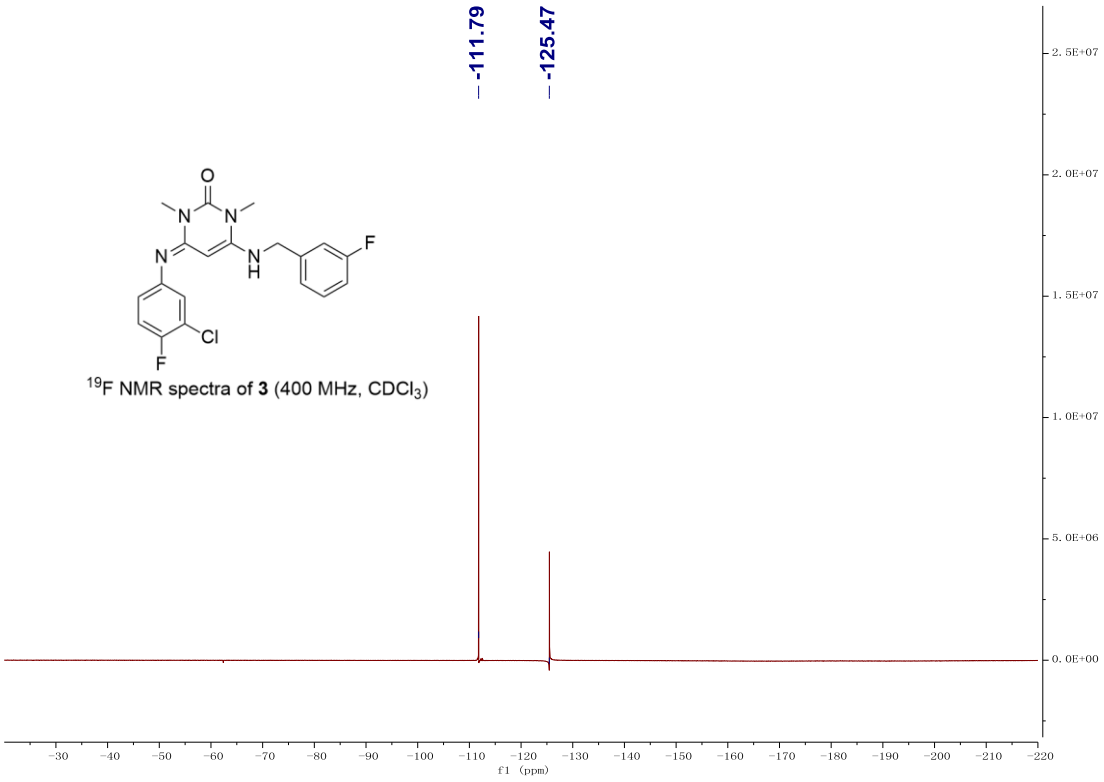




^{1}H NMR spectra of **3** (400 MHz, $CDCl_3$)



^{13}C {HNMR} spectra of **3** (101 MHz, $CDCl_3$)



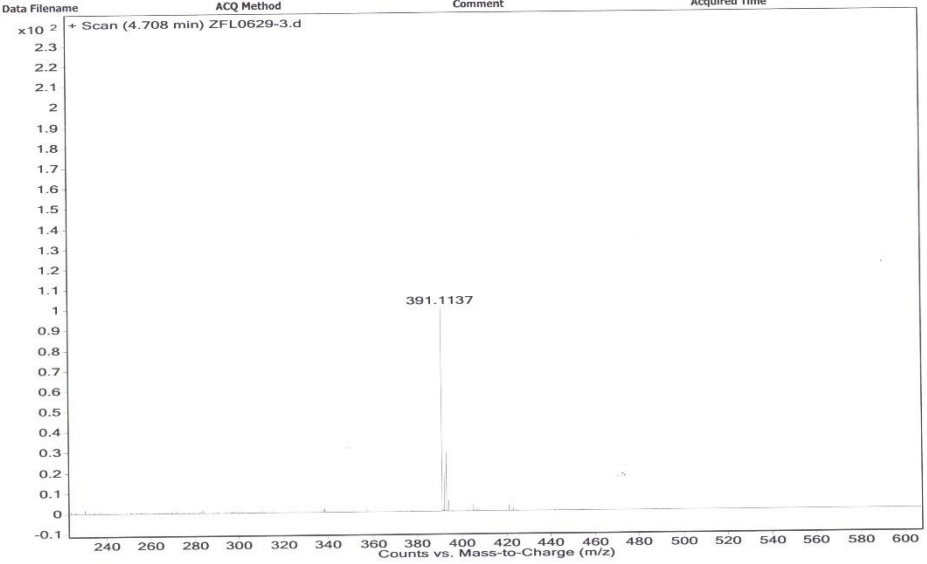
^{19}F NMR spectra of **3** (400 MHz, $CDCl_3$)

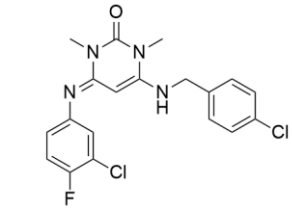
Sample Name
Inj Vol
Data Filename

Position
InjPosition
ACQ Method

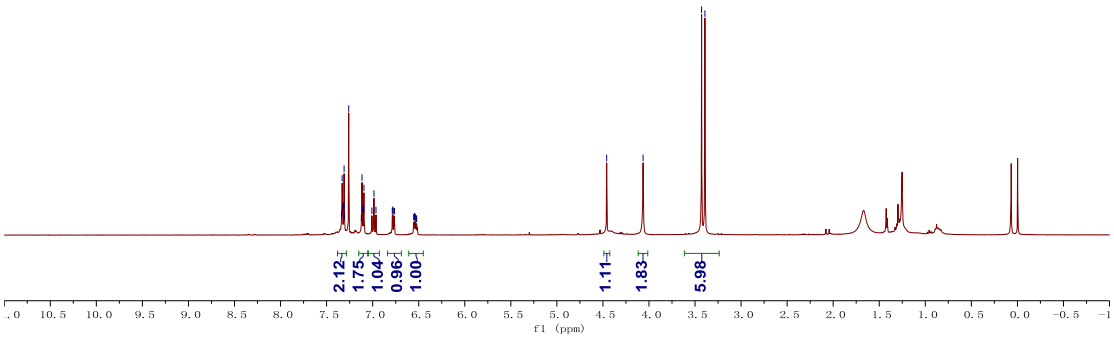
Instrument Name
SampleType
Comment

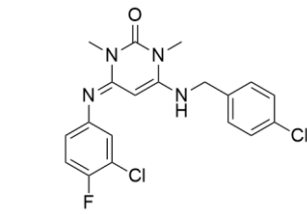
User Name
IRM Calibration Status
Acquired Time



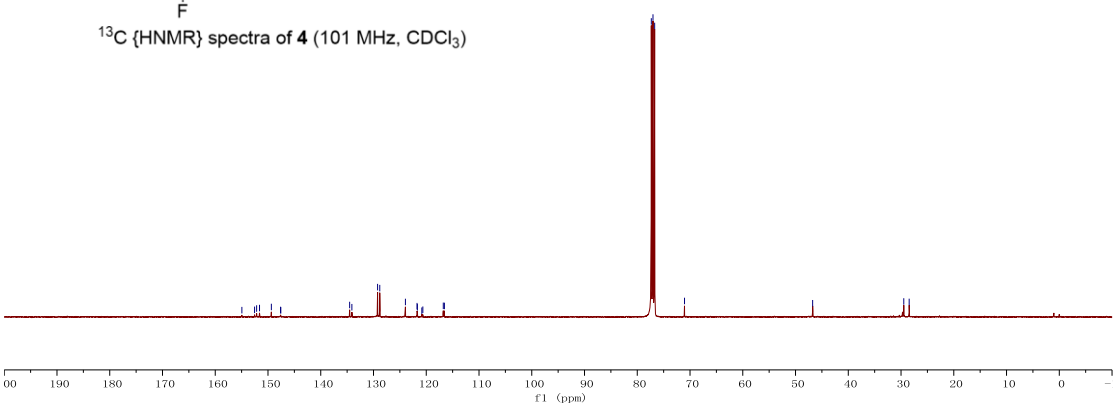


^{1}H NMR spectra of **4** (400 MHz, $CDCl_3$)

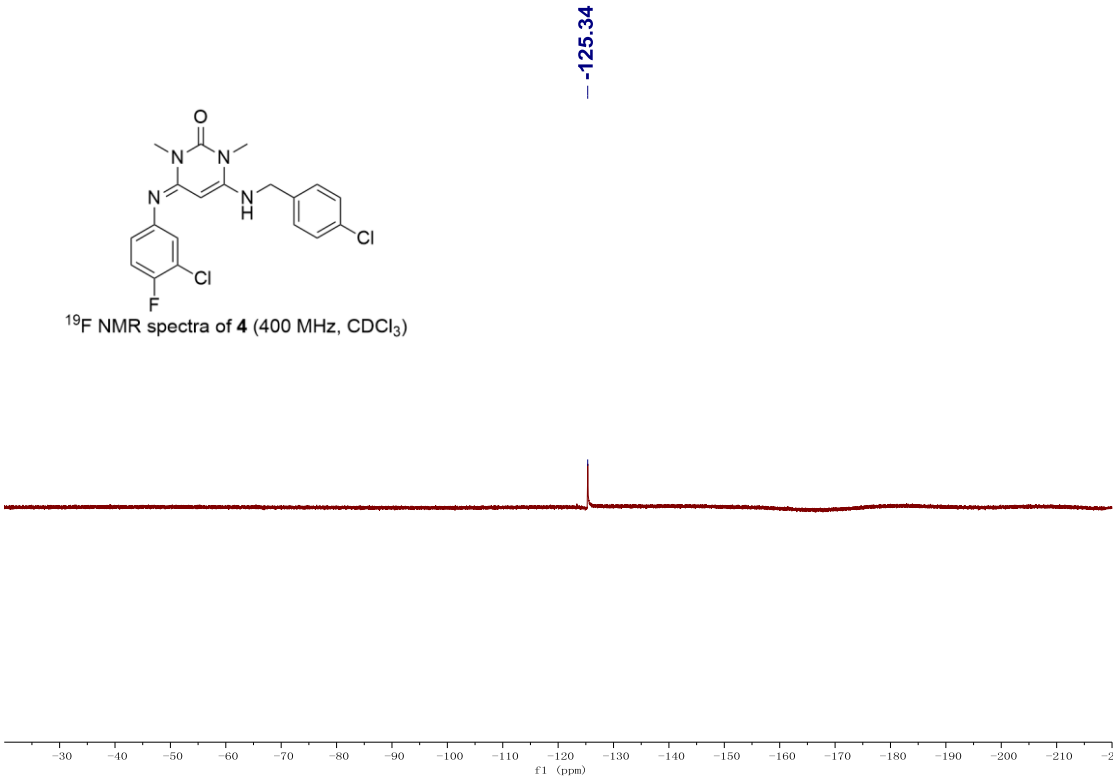


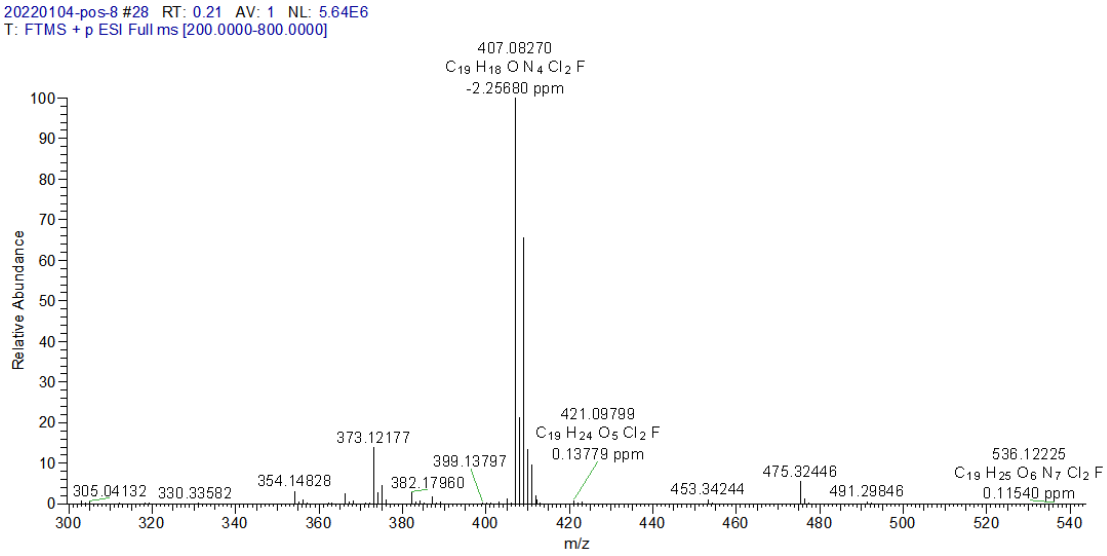


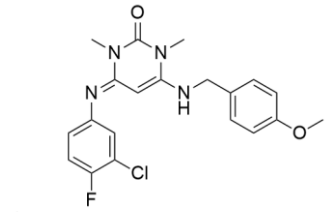
^{13}C {HNMR} spectra of **4** (101 MHz, $CDCl_3$)



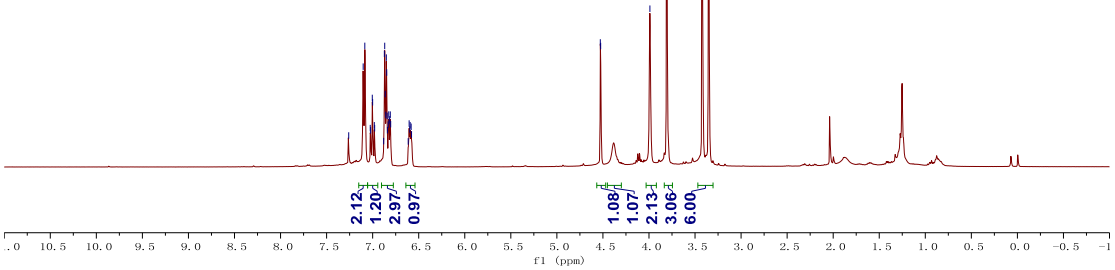
^{19}F NMR spectra of **4** (400 MHz, $CDCl_3$)

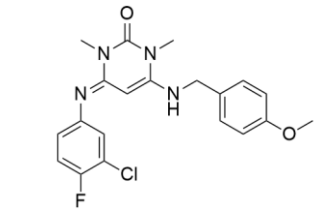




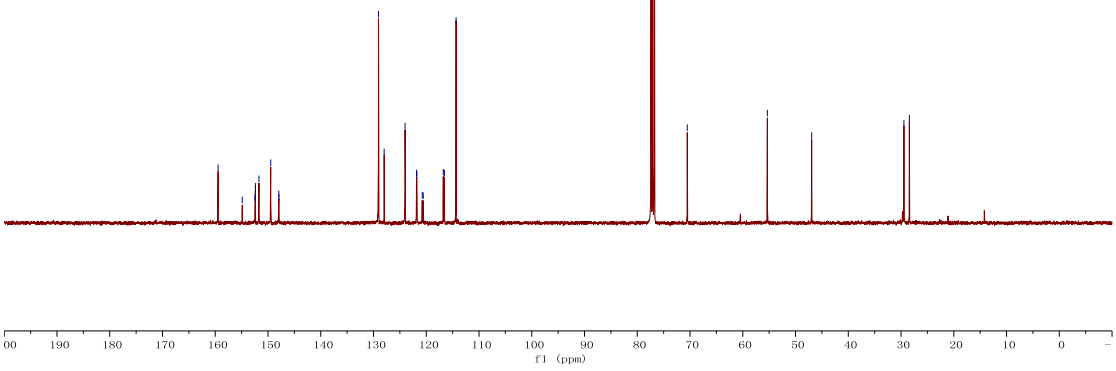


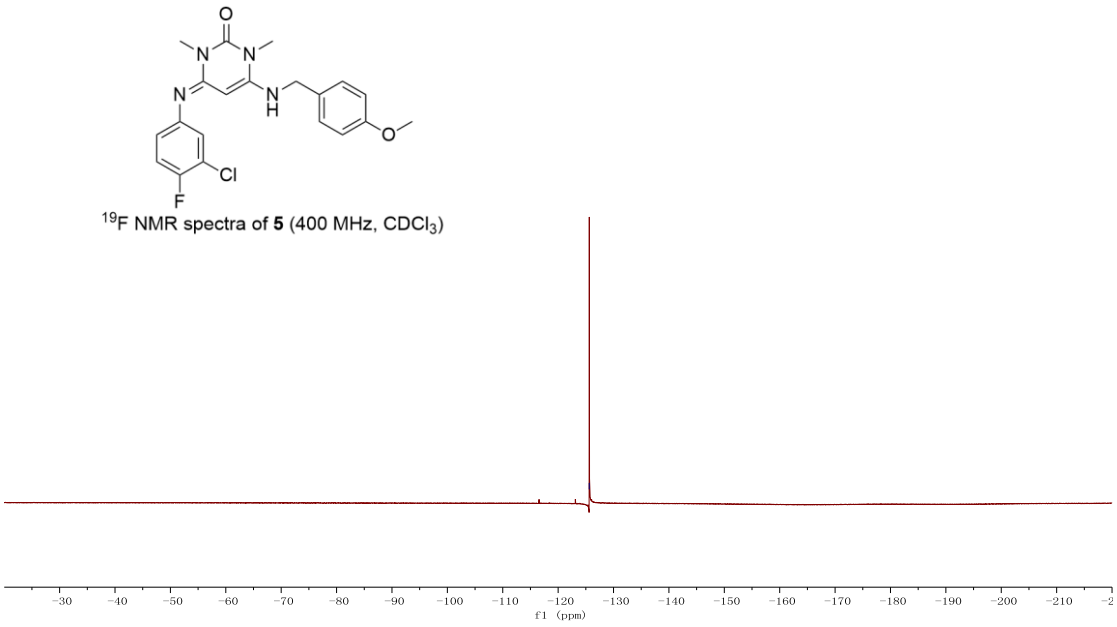
^{1}H NMR spectra of **5** (400 MHz, $CDCl_3$)





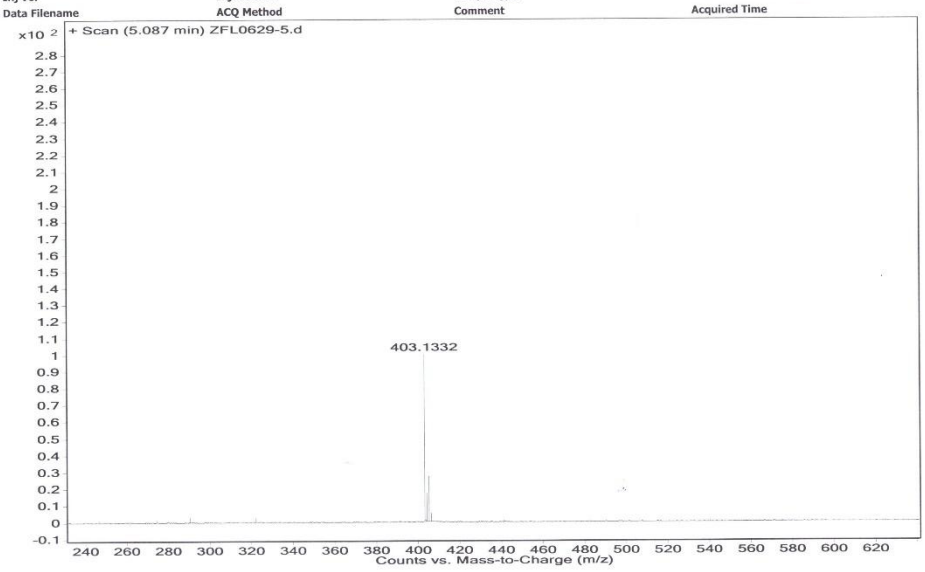
^{13}C {HNMR} spectra of **5** (101 MHz, $CDCl_3$)

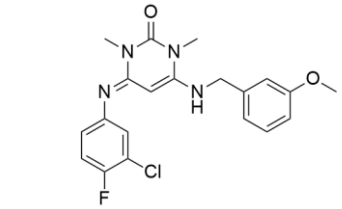




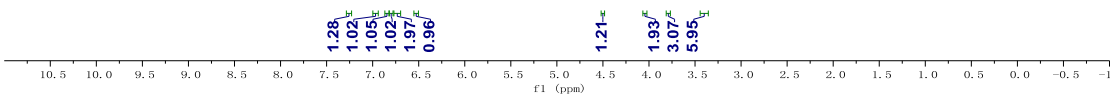
^{19}F NMR spectra of **5** (400 MHz, $CDCl_3$)

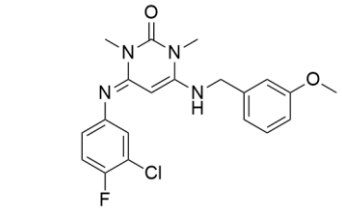
Sample Name	Position	Instrument Name	User Name
Inj Vol	InjPosition	SampleType	IRM Calibration Status
Data Filename	ACQ Method	Comment	Acquired Time



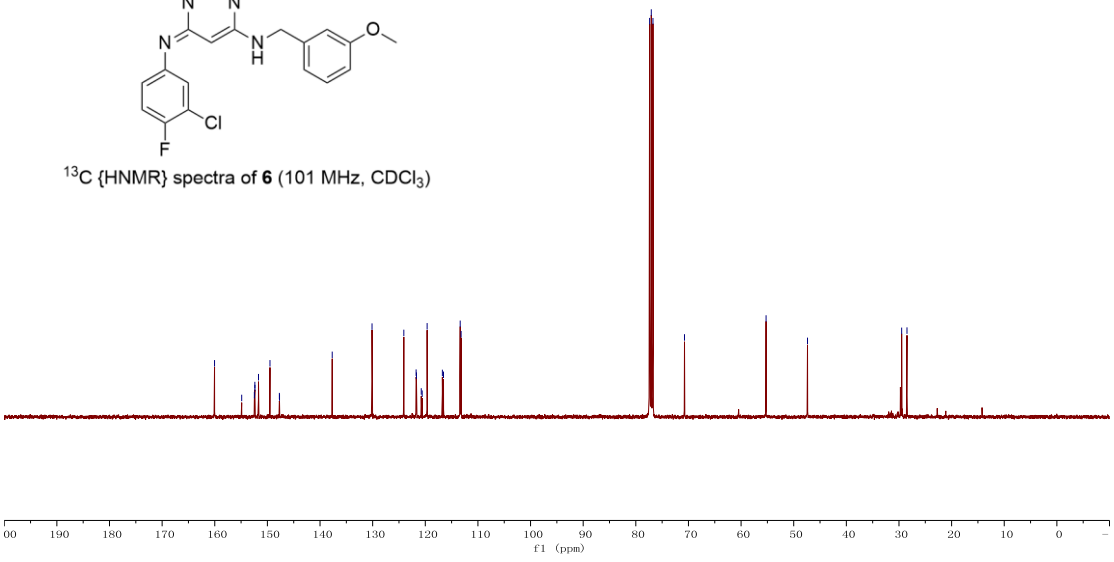


^{1}H NMR spectra of **6** (400 MHz, $CDCl_3$)

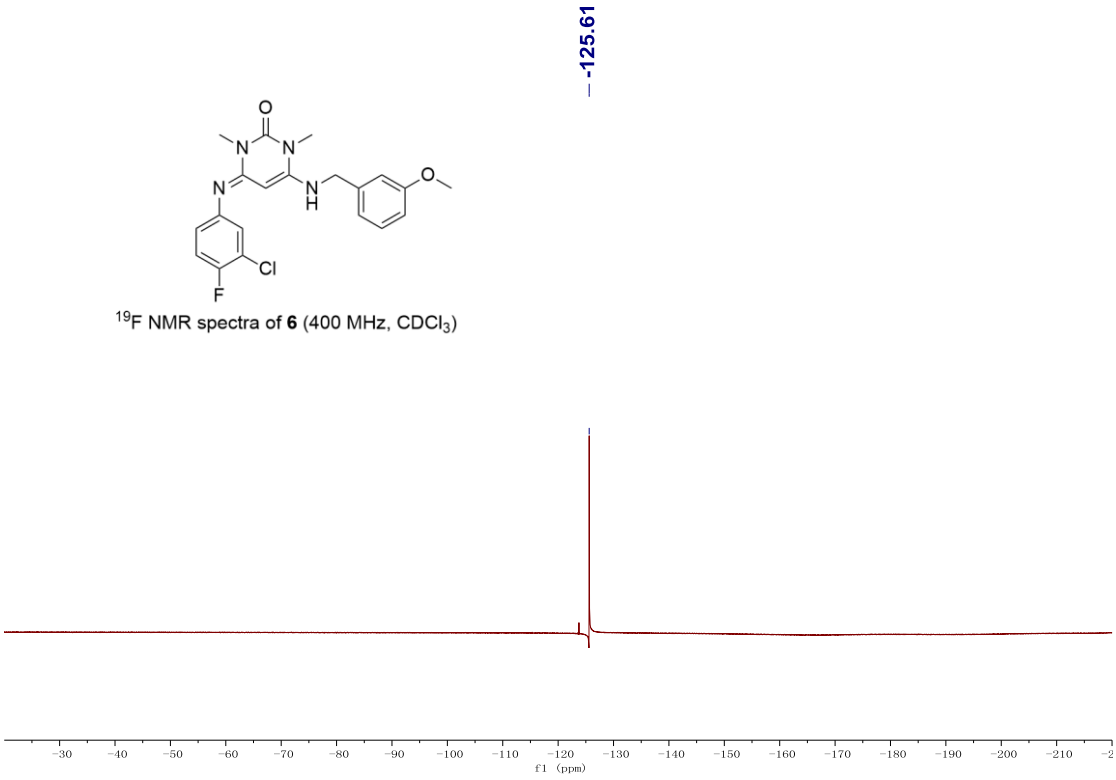




^{13}C {HNMR} spectra of **6** (101 MHz, $CDCl_3$)

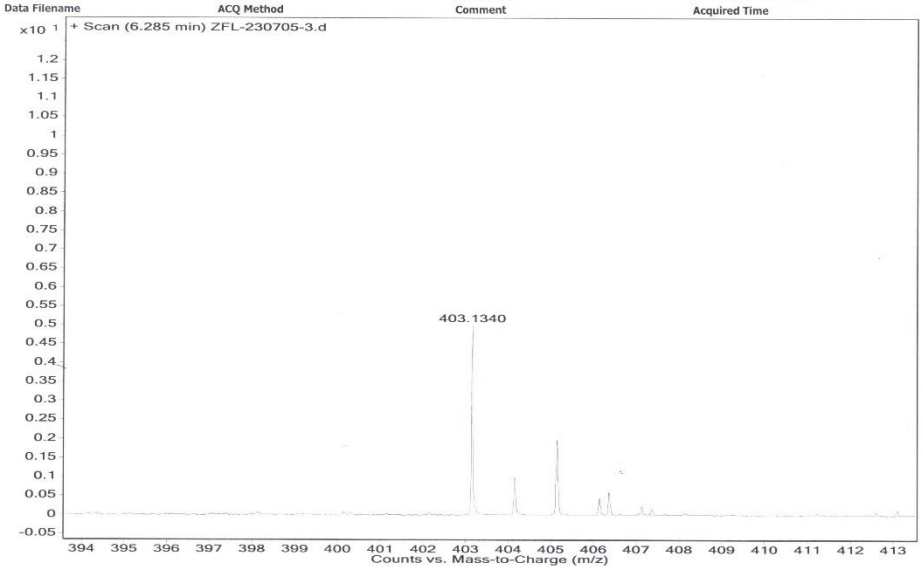


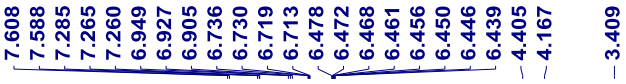
^{19}F NMR spectra of **6** (400 MHz, $CDCl_3$)

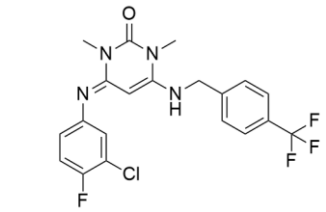


18.

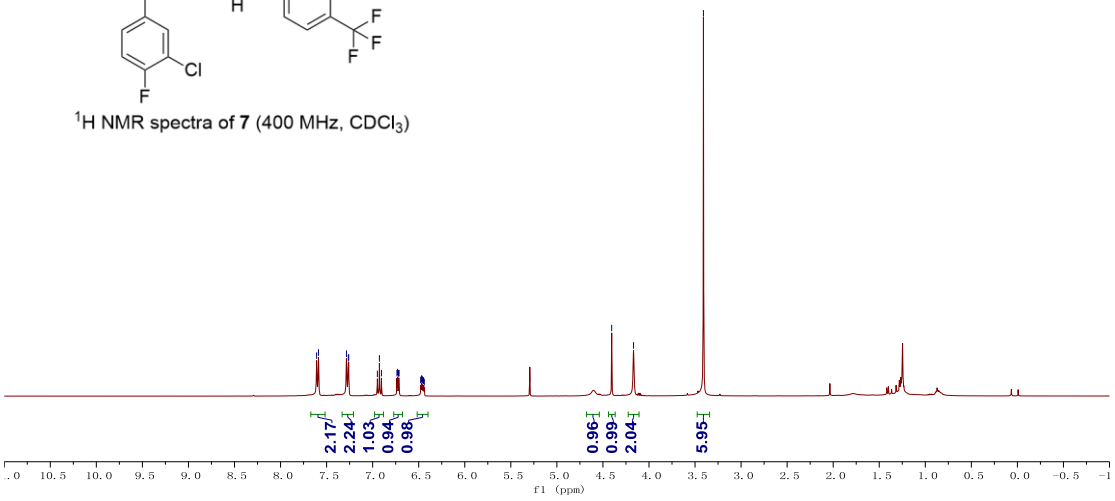
Sample Name	Position	Instrument Name	User Name
Inj Vol	InjPosition	SampleType	IRM Calibration Status
Data Filename	ACQ Method	Comment	Acquired Time

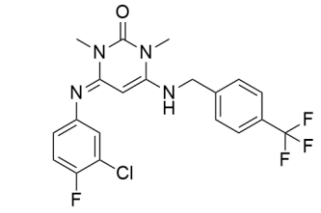




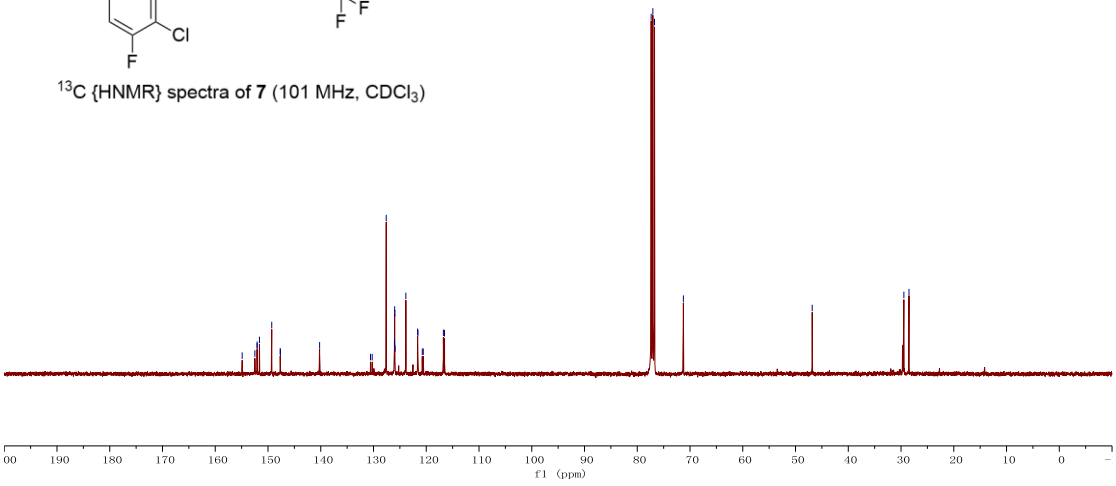


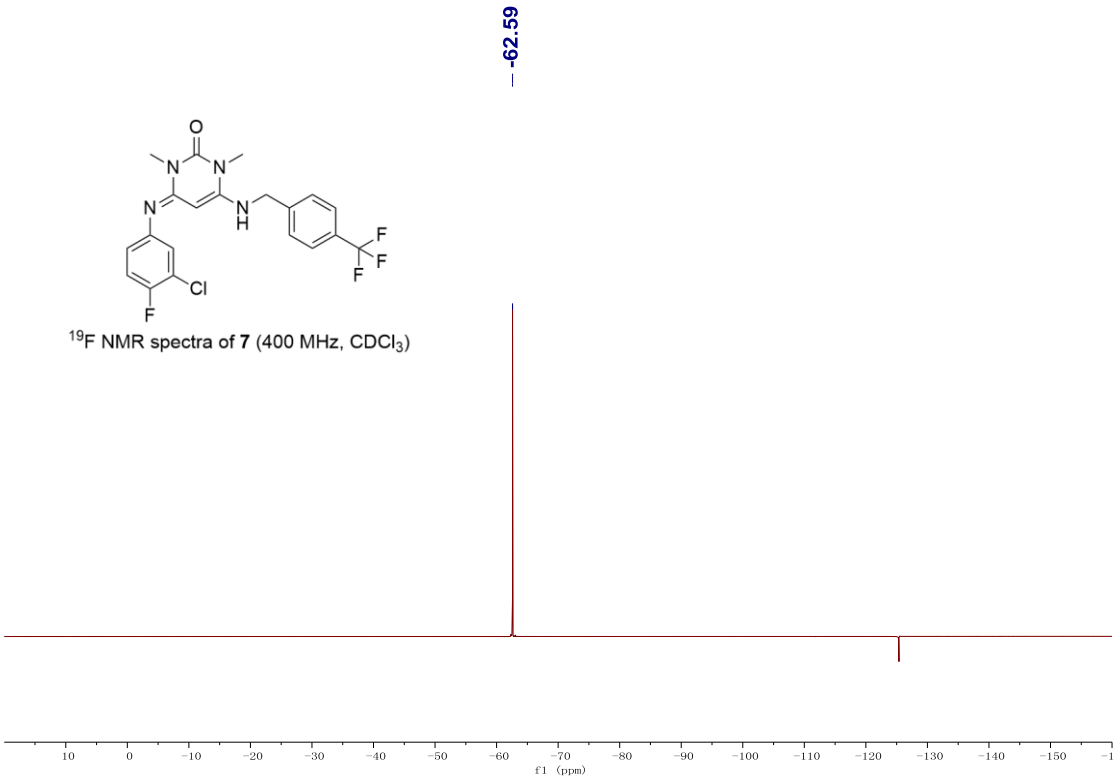
^{1}H NMR spectra of **7** (400 MHz, $CDCl_3$)





^{13}C {HNMR} spectra of **7** (101 MHz, $CDCl_3$)

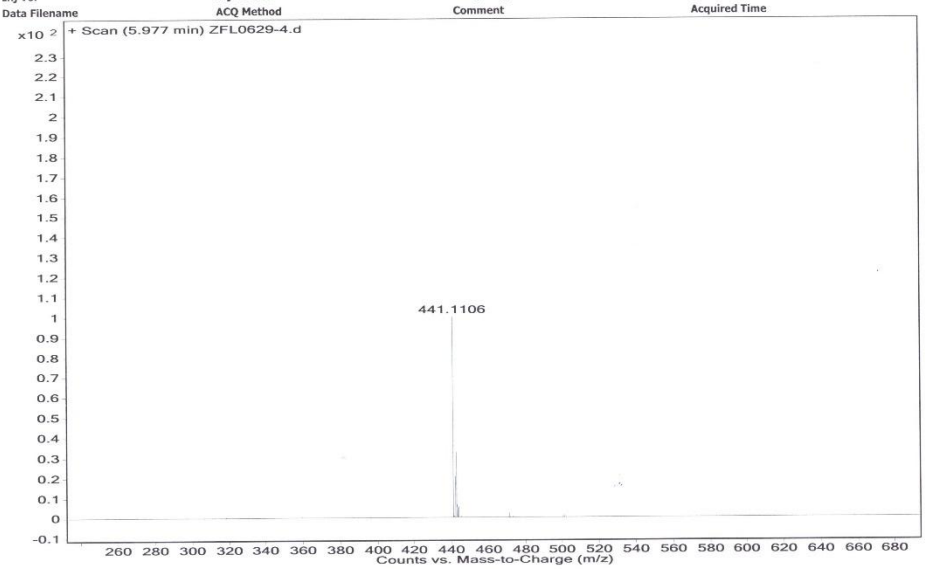


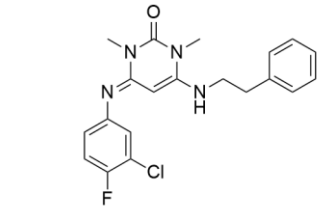


^{19}F NMR spectra of **7** (400 MHz, $CDCl_3$)

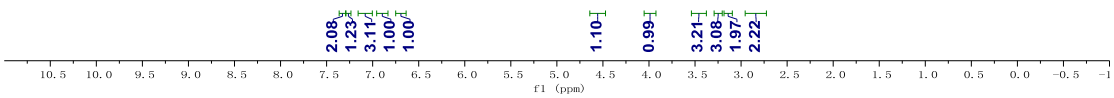
4.

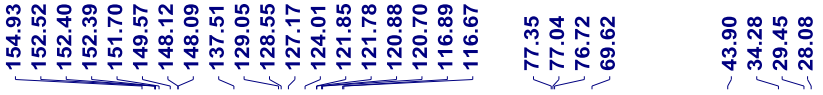
Sample Name	Position	Instrument Name	User Name
Inj Vol	InjPosition	SampleType	IRM Calibration Status
Data Filename	ACQ Method	Comment	Acquired Time

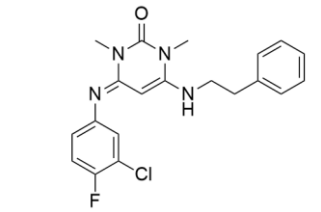




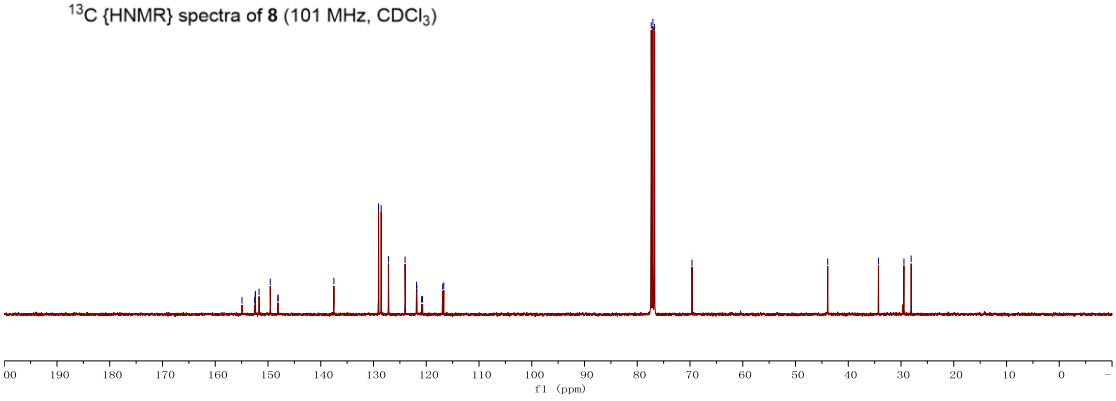
^{1}H NMR spectra of **8** (400 MHz, $CDCl_3$)

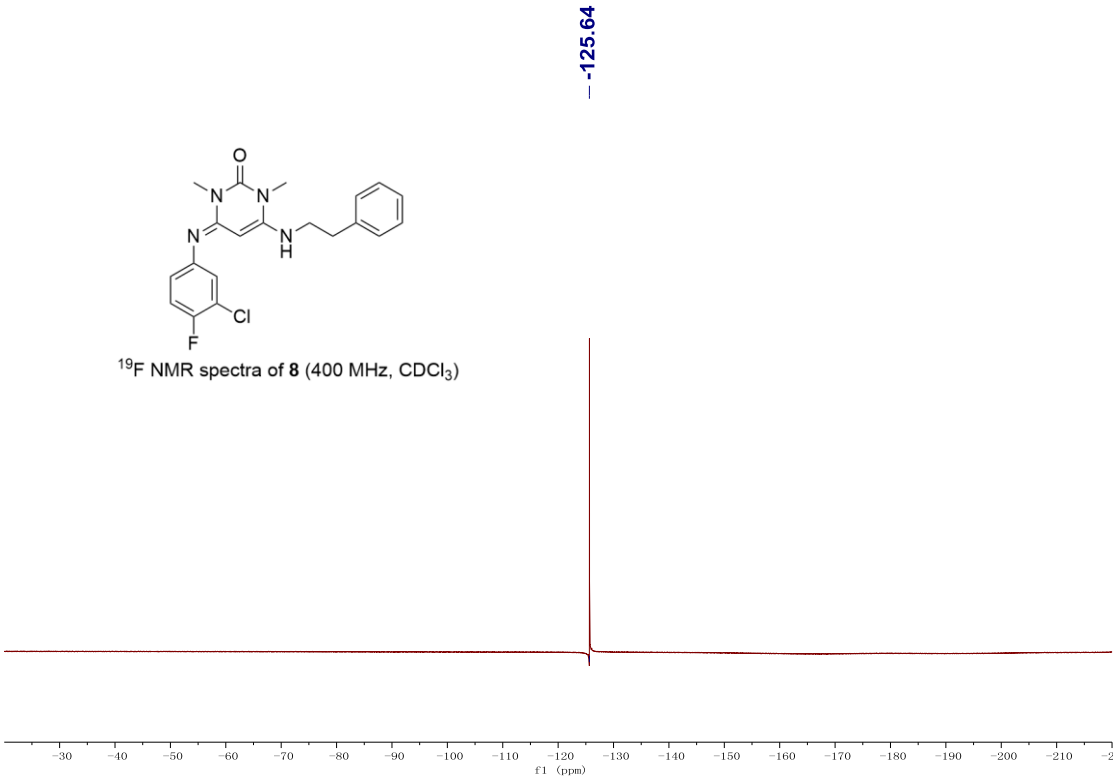




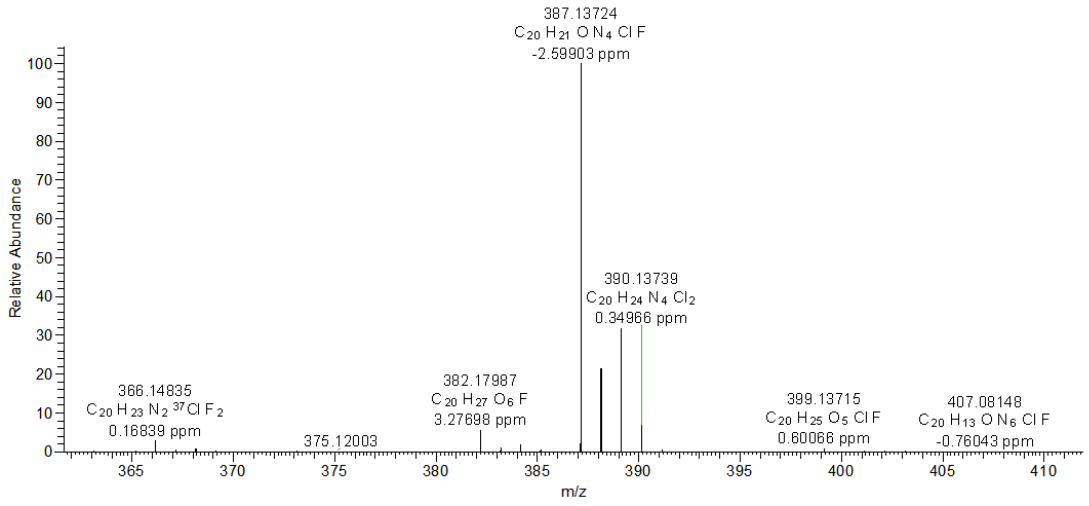


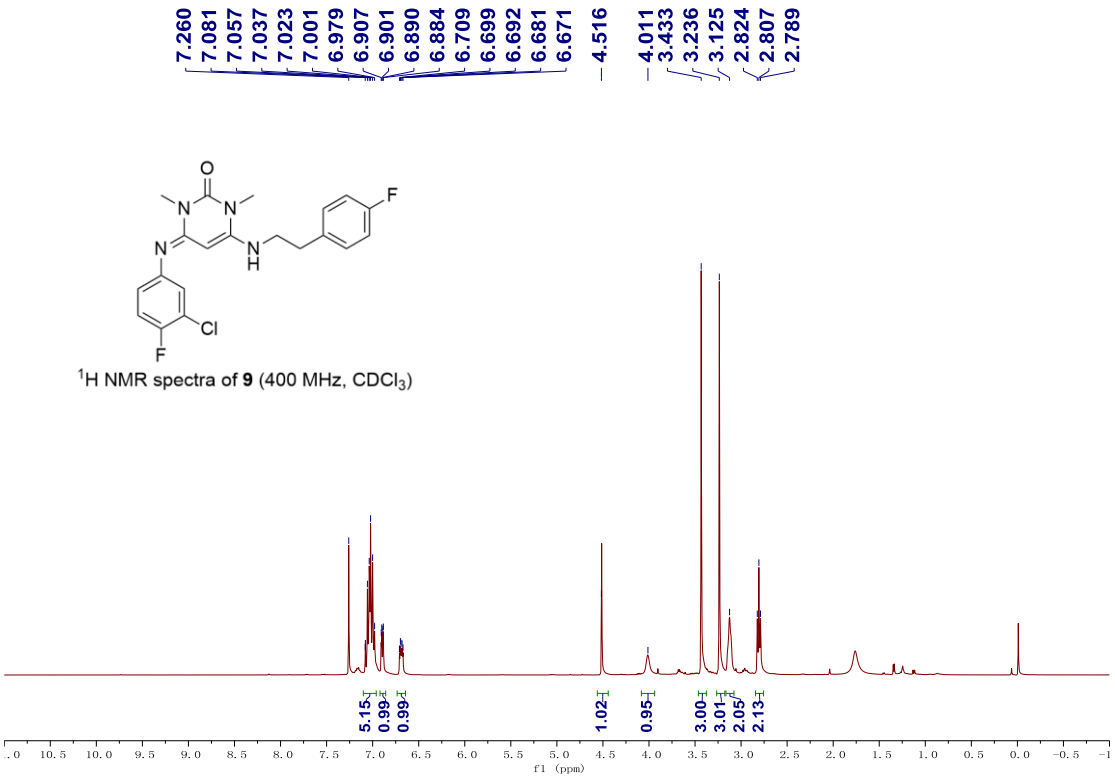
^{13}C {HNMR} spectra of **8** (101 MHz, $CDCl_3$)



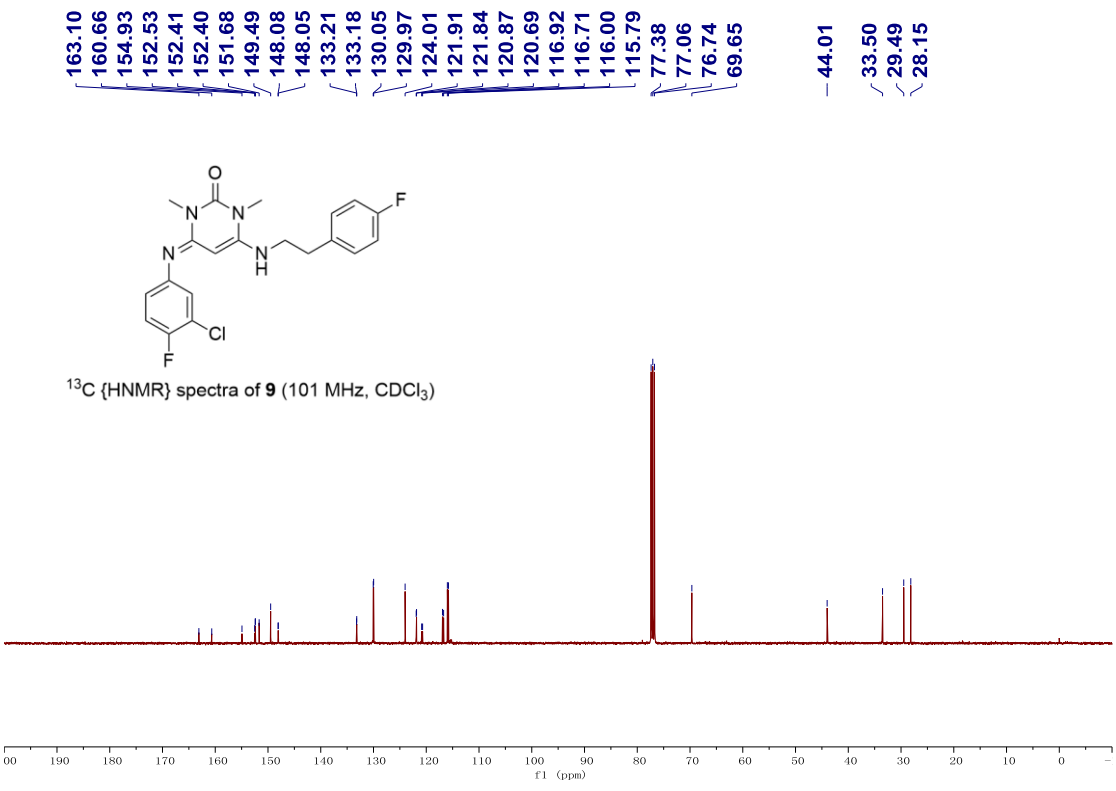


^{19}F NMR spectra of **8** (400 MHz, $CDCl_3$)

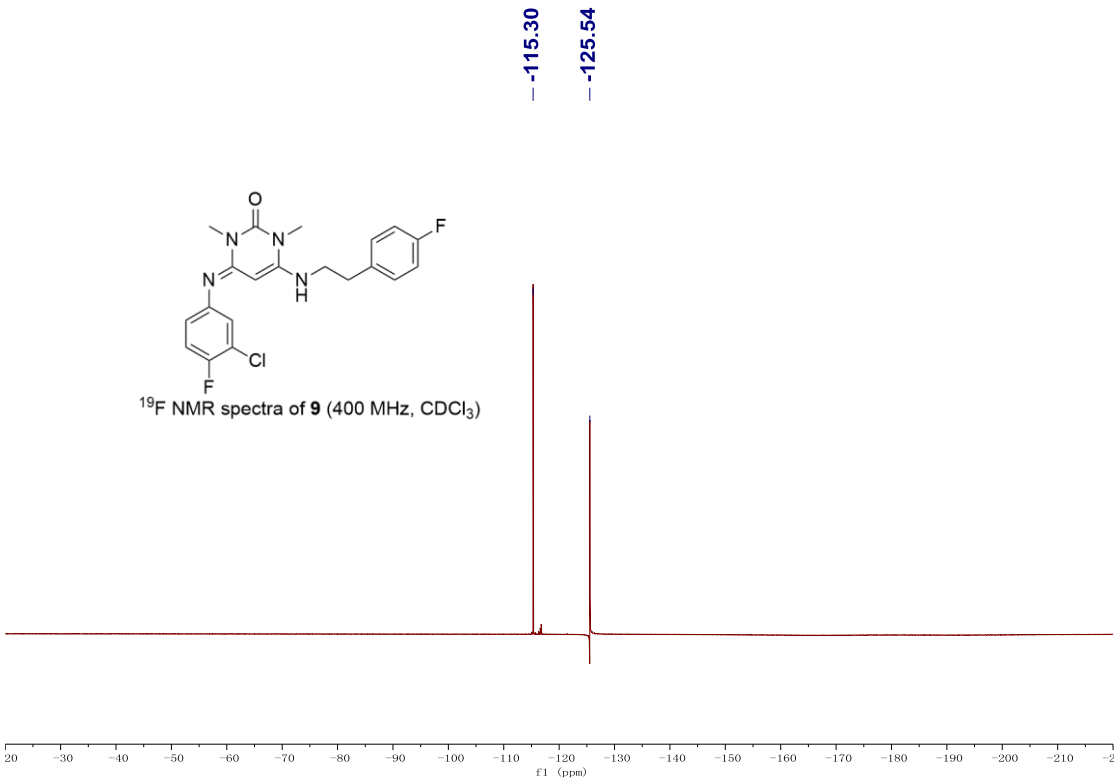




^{1}H NMR spectra of **9** (400 MHz, $CDCl_3$)

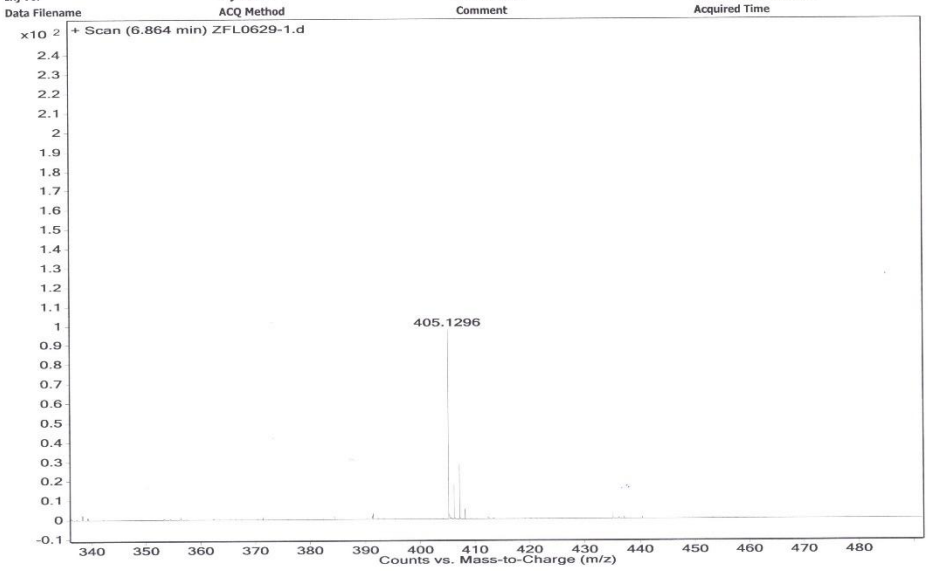


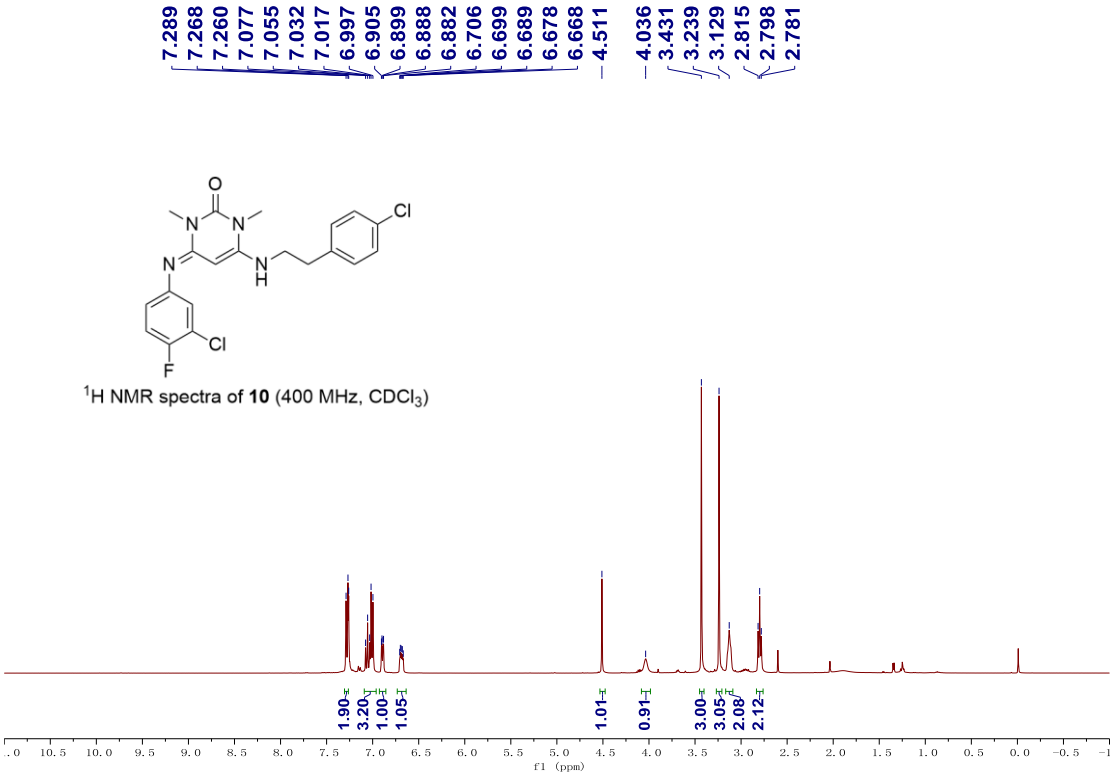
^{13}C {HNMR} spectra of **9** (101 MHz, $CDCl_3$)



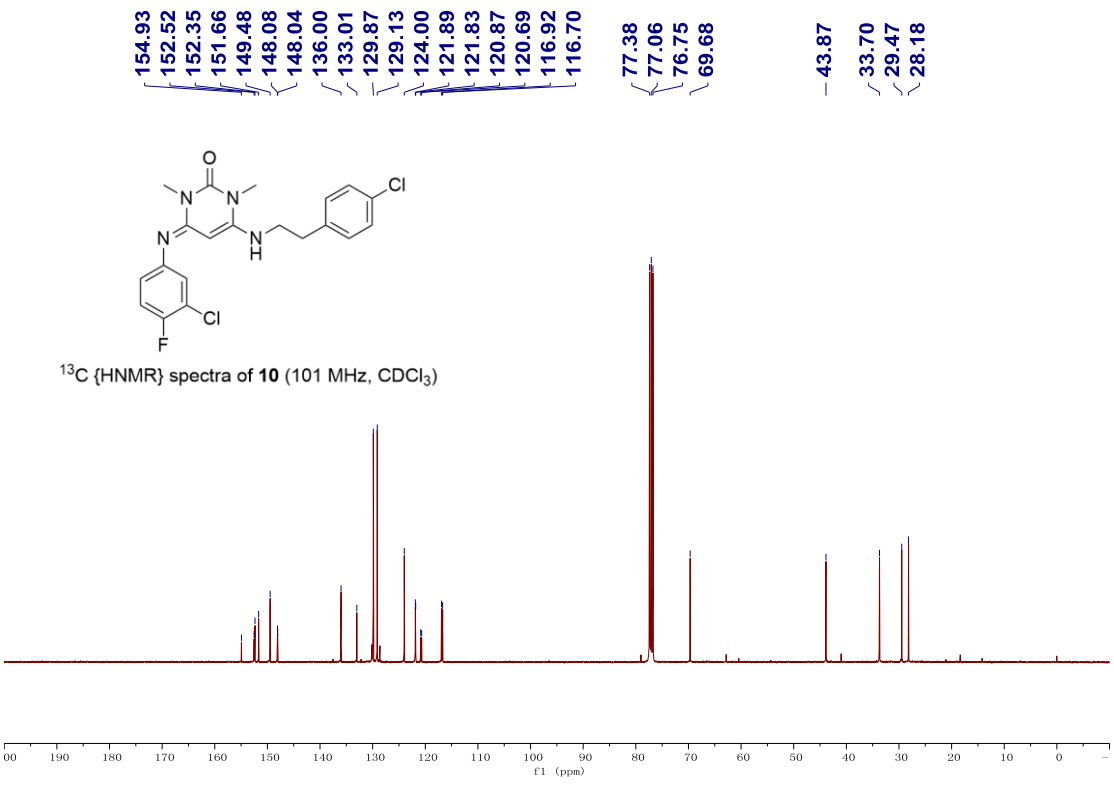
^{19}F NMR spectra of **9** (400 MHz, $CDCl_3$)

Sample Name	Position	Instrument Name	User Name
Inj Vol	InjPosition	SampleType	IRM Calibration Status
Data Filename	ACQ Method	Comment	Acquired Time



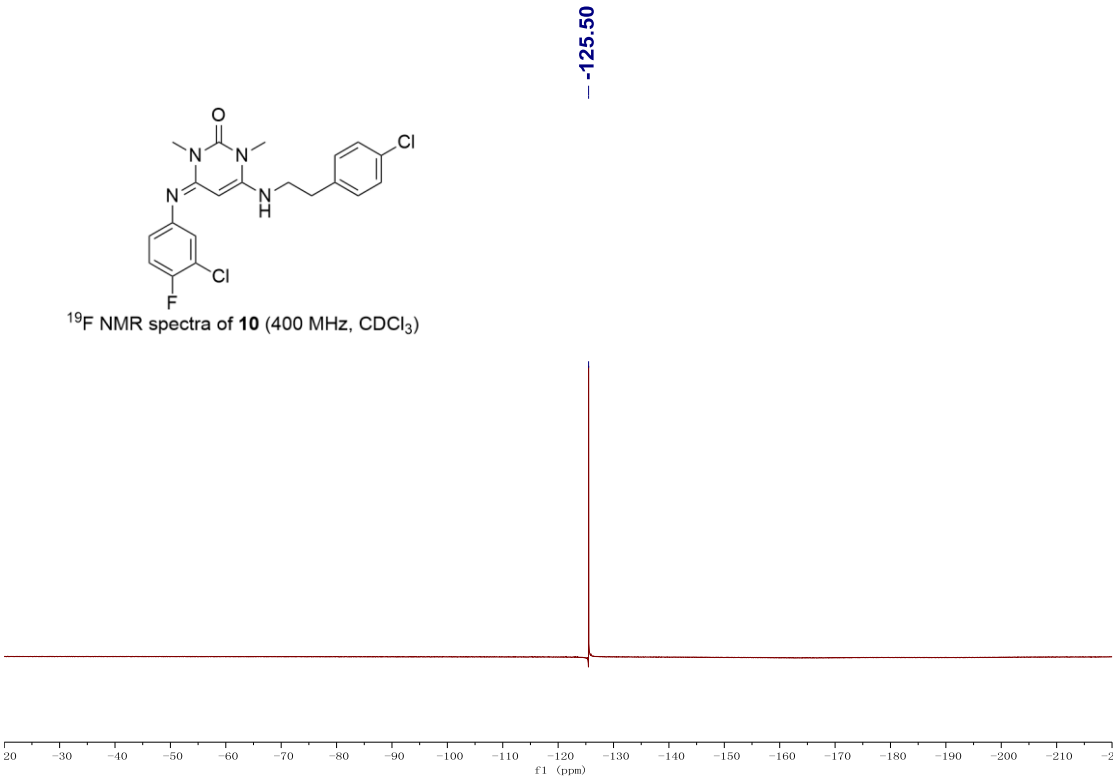


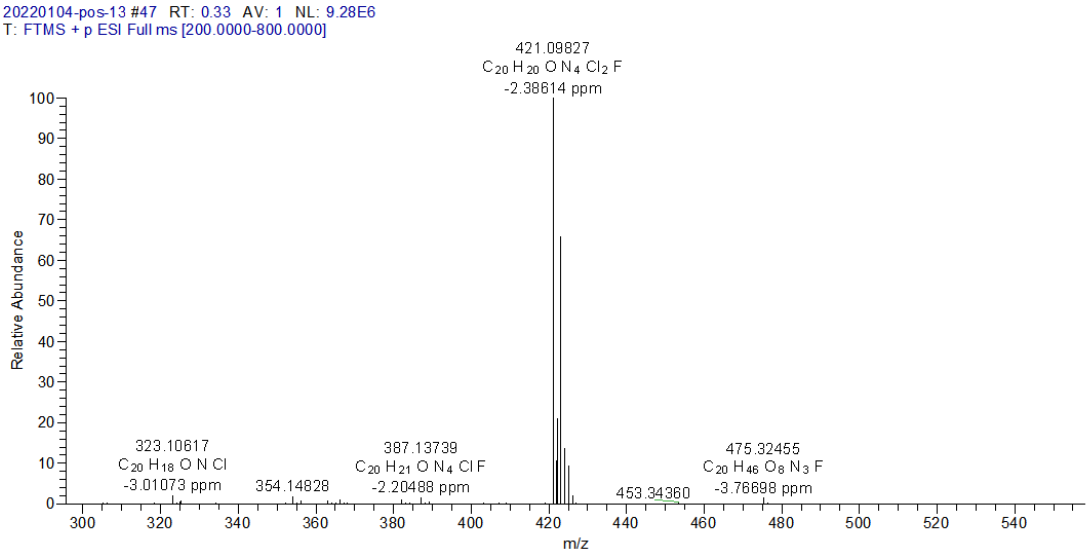
^{1}H NMR spectra of **10** (400 MHz, $CDCl_3$)

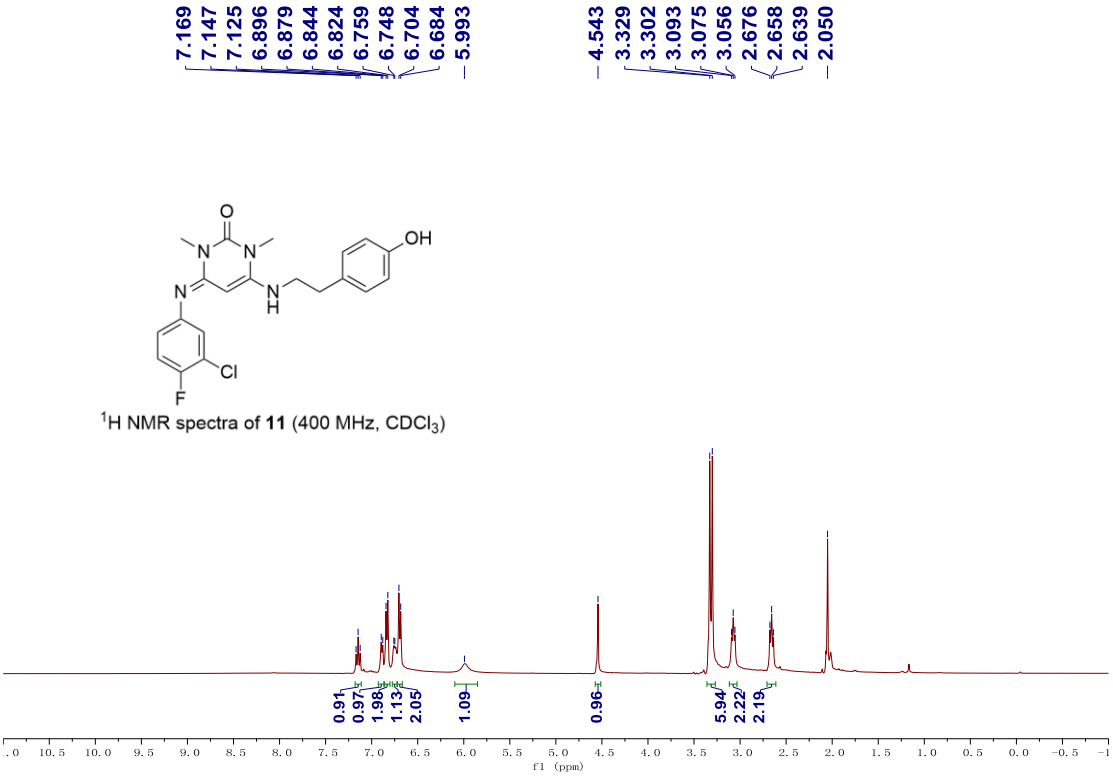


^{13}C {HNMR} spectra of **10** (101 MHz, $CDCl_3$)

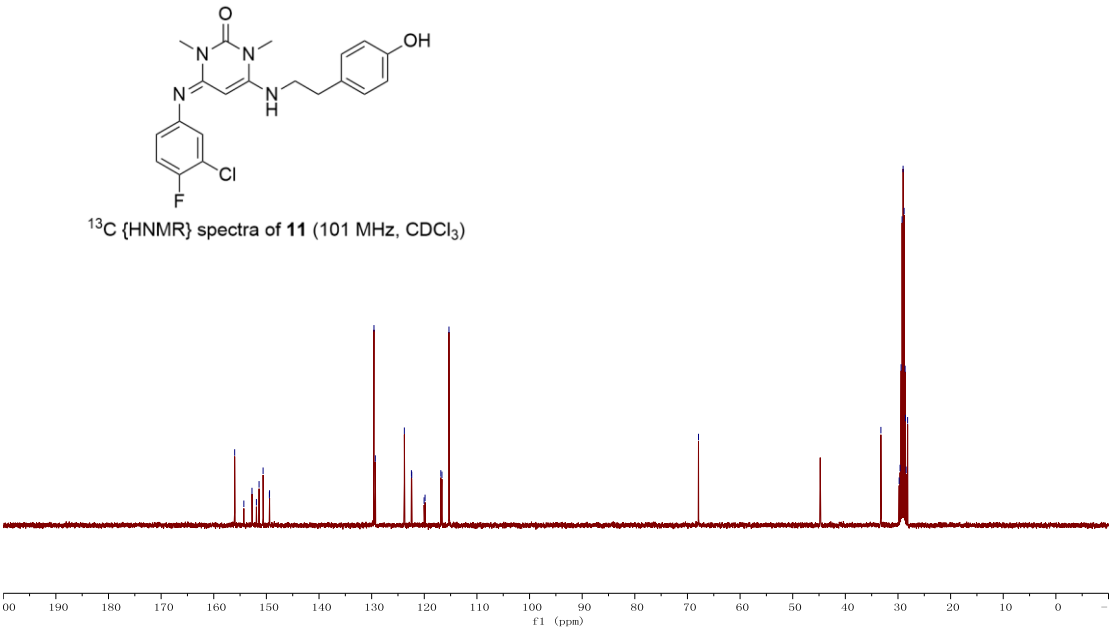
^{19}F NMR spectra of **10** (400 MHz, $CDCl_3$)



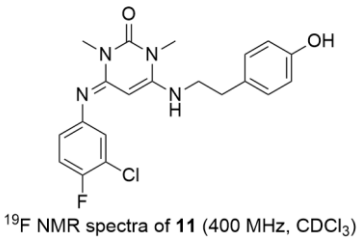




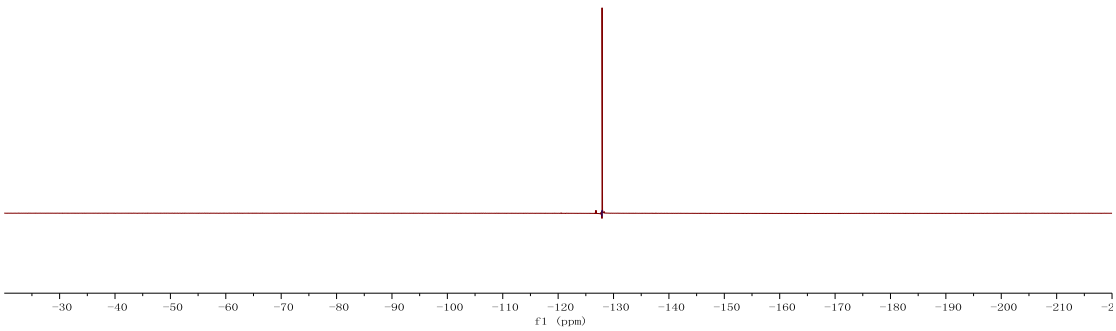
^{1}H NMR spectra of **11** (400 MHz, $CDCl_3$)



^{13}C {HNMR} spectra of **11** (101 MHz, $CDCl_3$)



^{19}F NMR spectra of **11** (400 MHz, $CDCl_3$)



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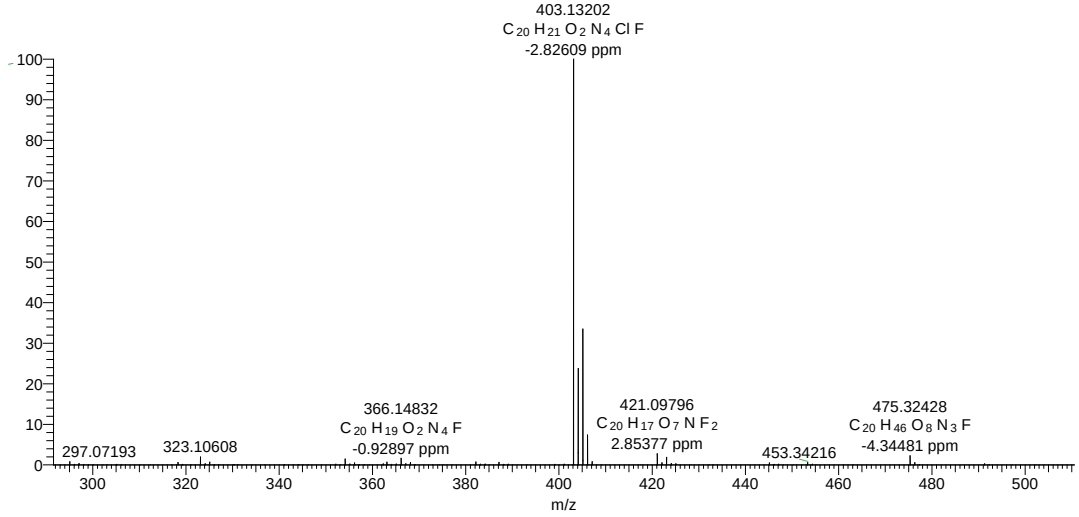
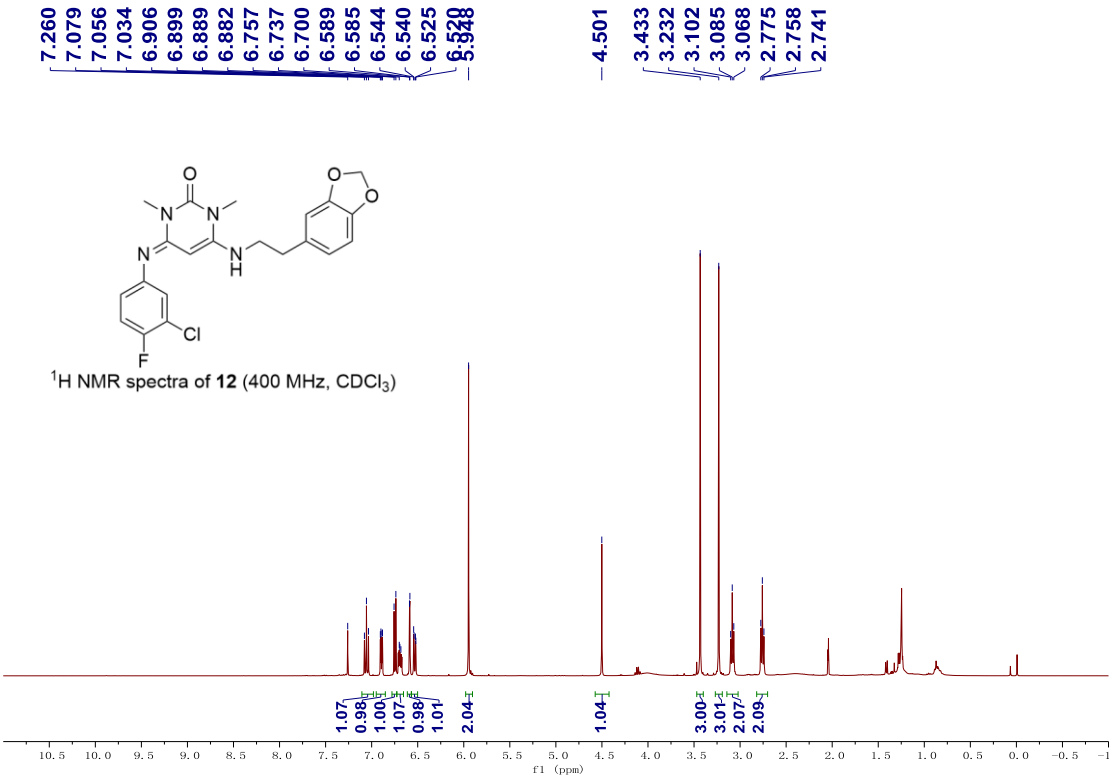
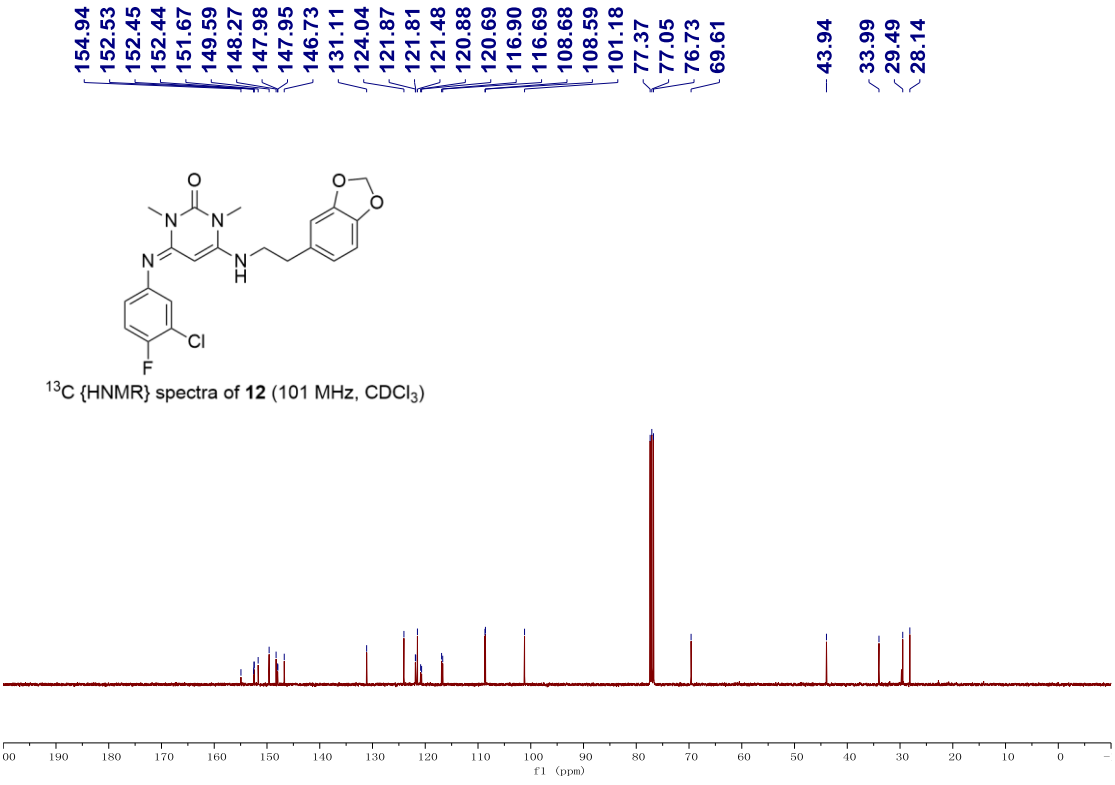
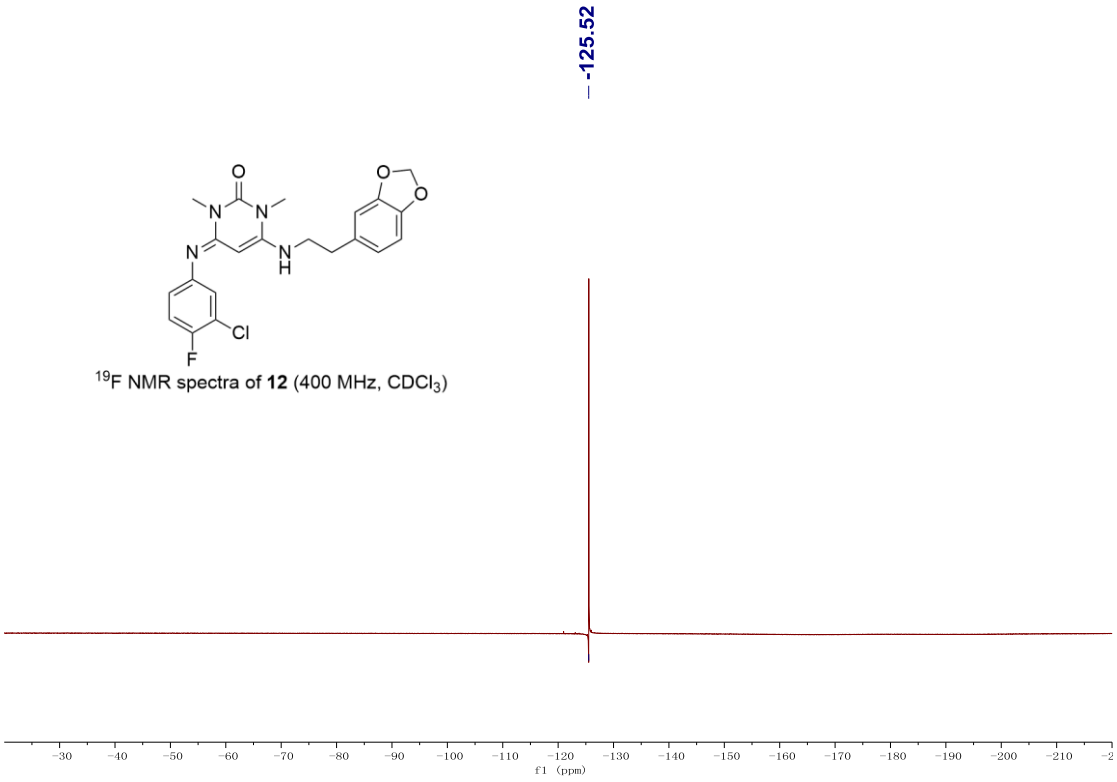




^{1}H NMR spectra of **12** (400 MHz, $CDCl_3$)



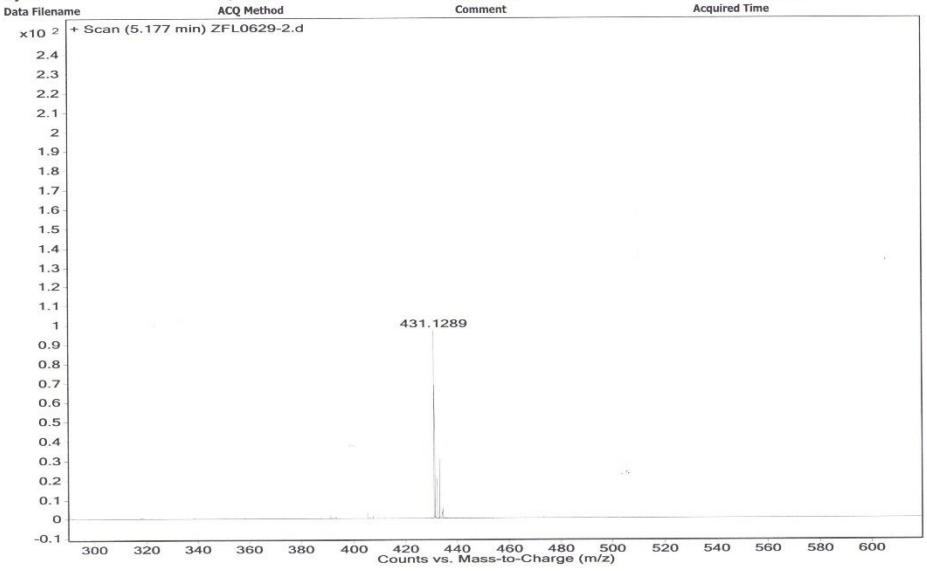
^{13}C {HNMR} spectra of **12** (101 MHz, $CDCl_3$)

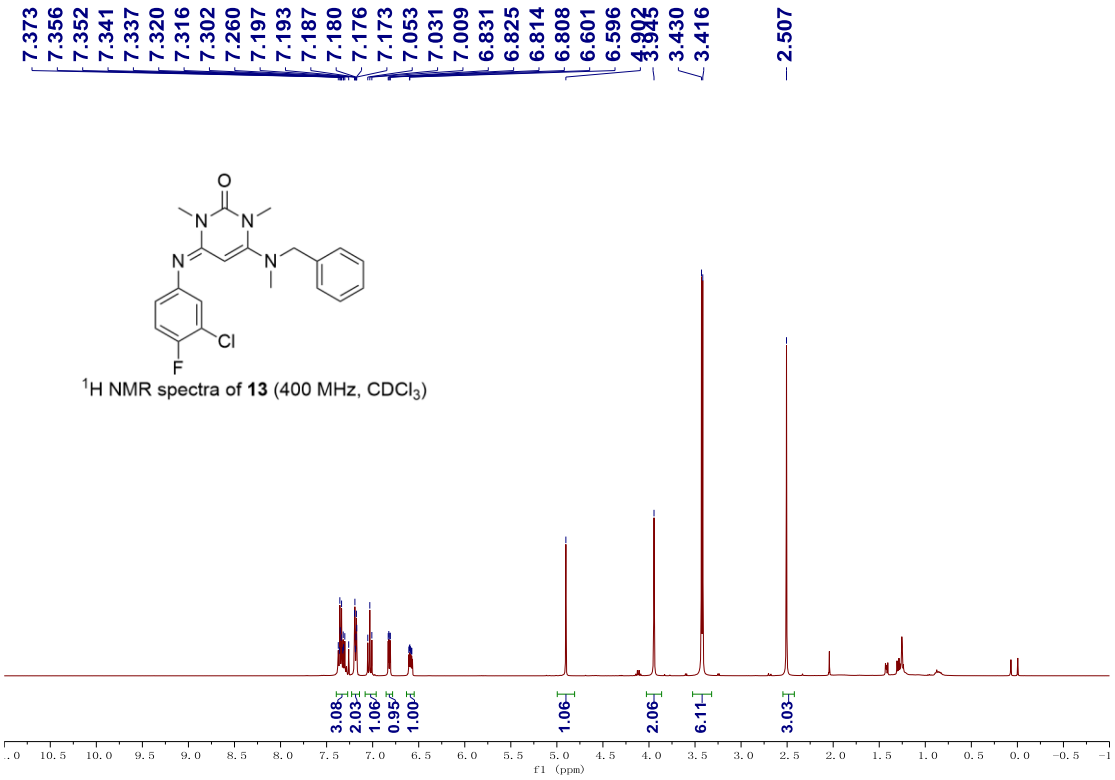


^{19}F NMR spectra of **12** (400 MHz, $CDCl_3$)

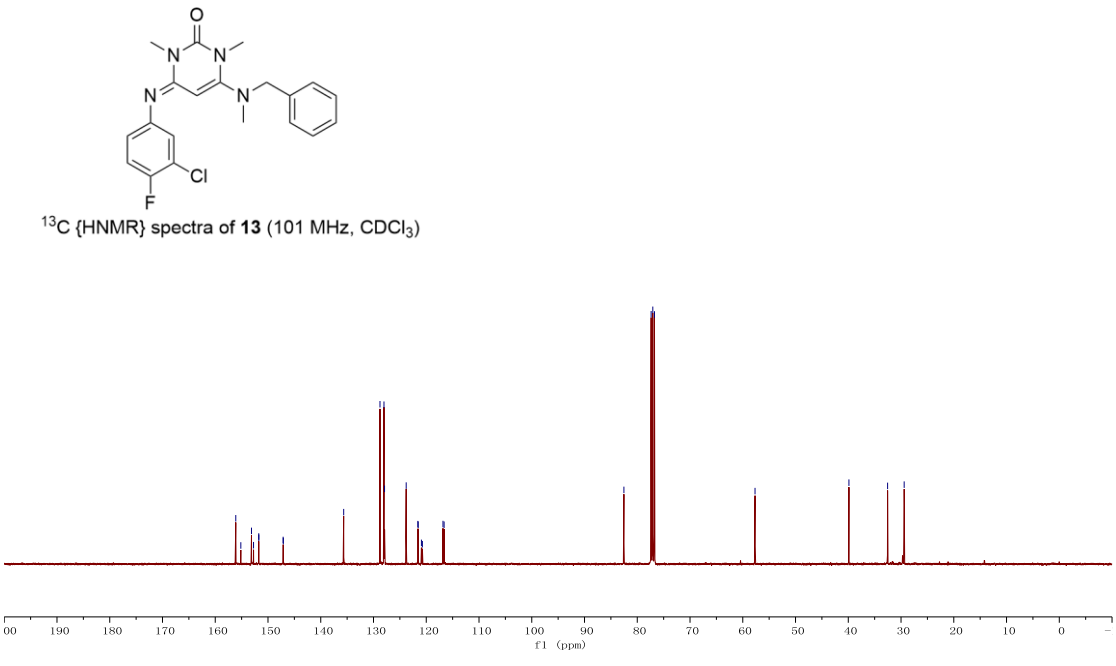
2.

Sample Name	Position	Instrument Name	User Name
Inj Vol	InjPosition	SampleType	IRM Calibration Status
Data Filename	ACQ Method	Comment	Acquired Time



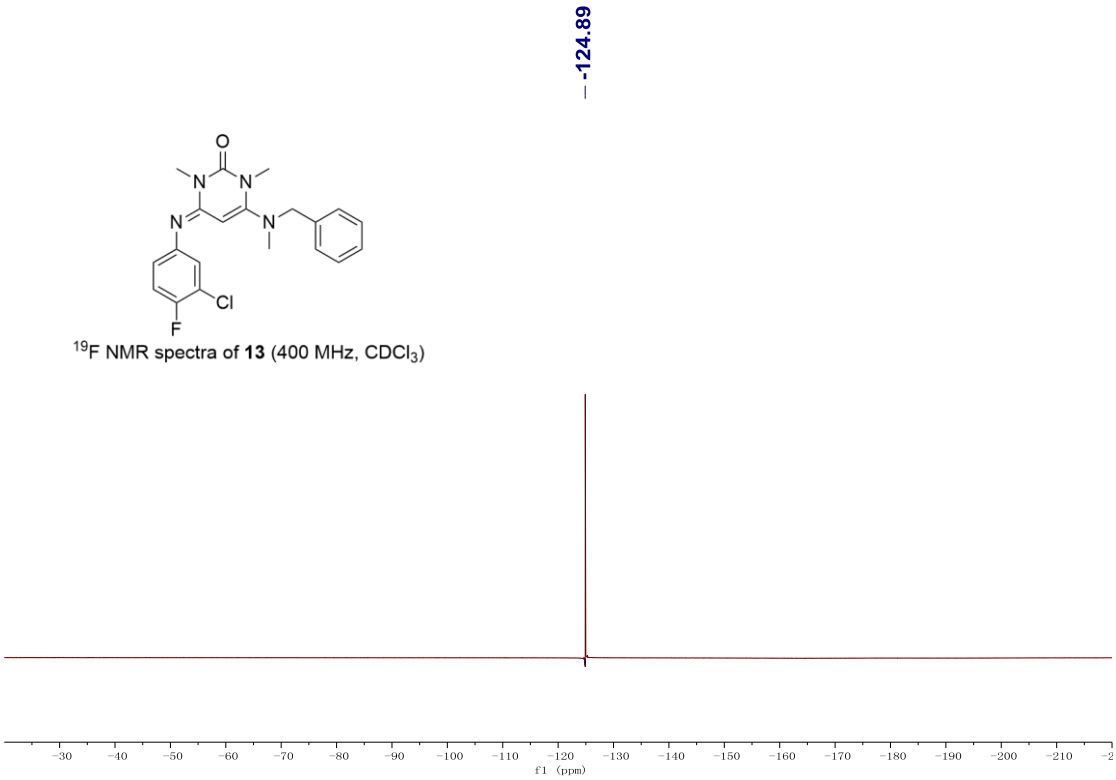


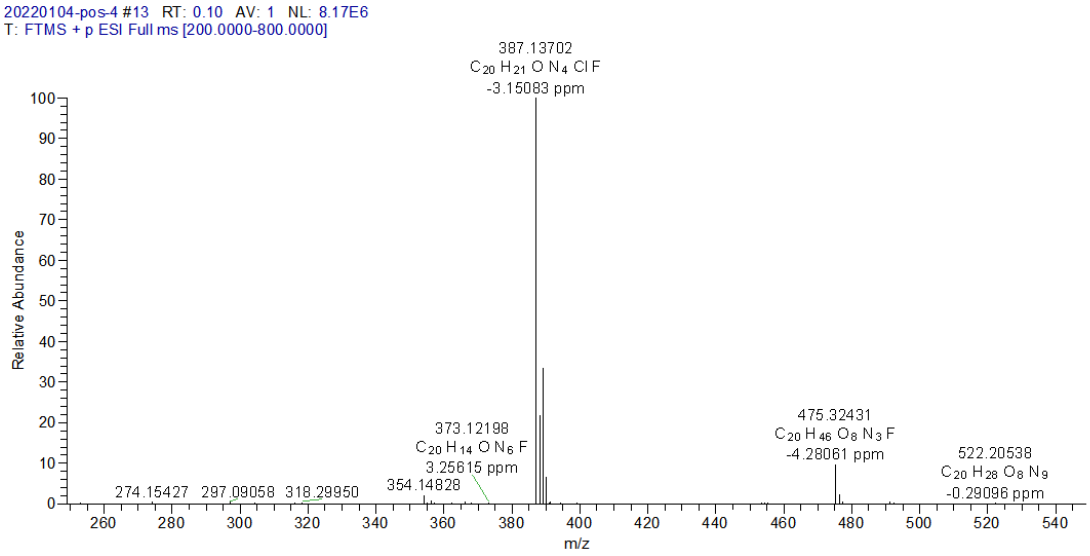
^{1}H NMR spectra of **13** (400 MHz, $CDCl_3$)

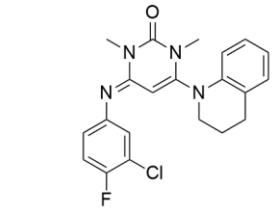


^{13}C {HNMR} spectra of **13** (101 MHz, $CDCl_3$)

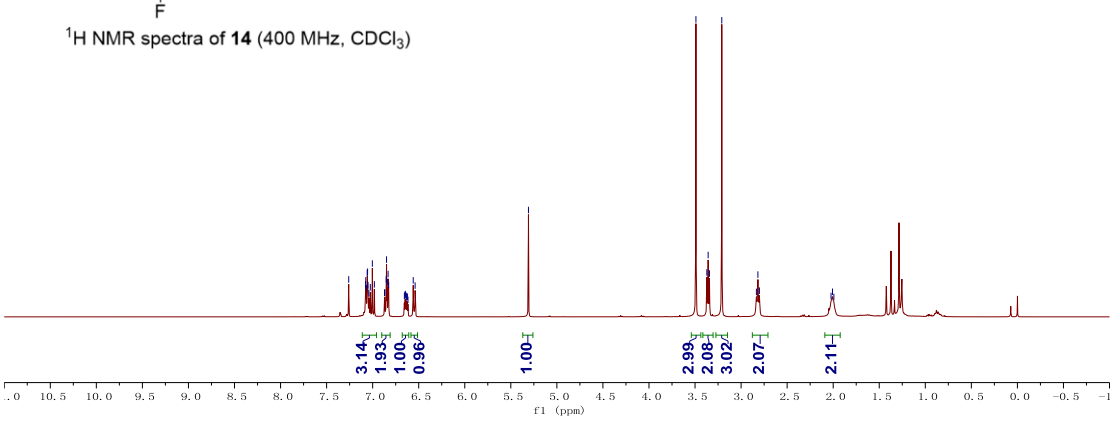
^{19}F NMR spectra of **13** (400 MHz, $CDCl_3$)

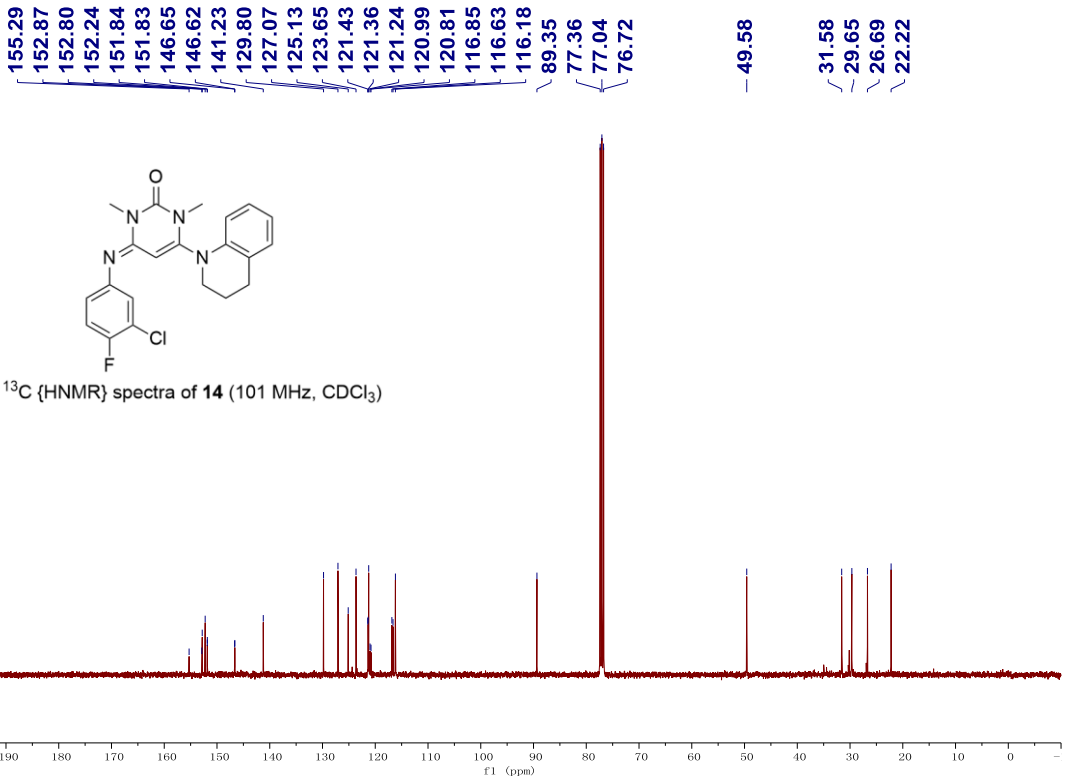




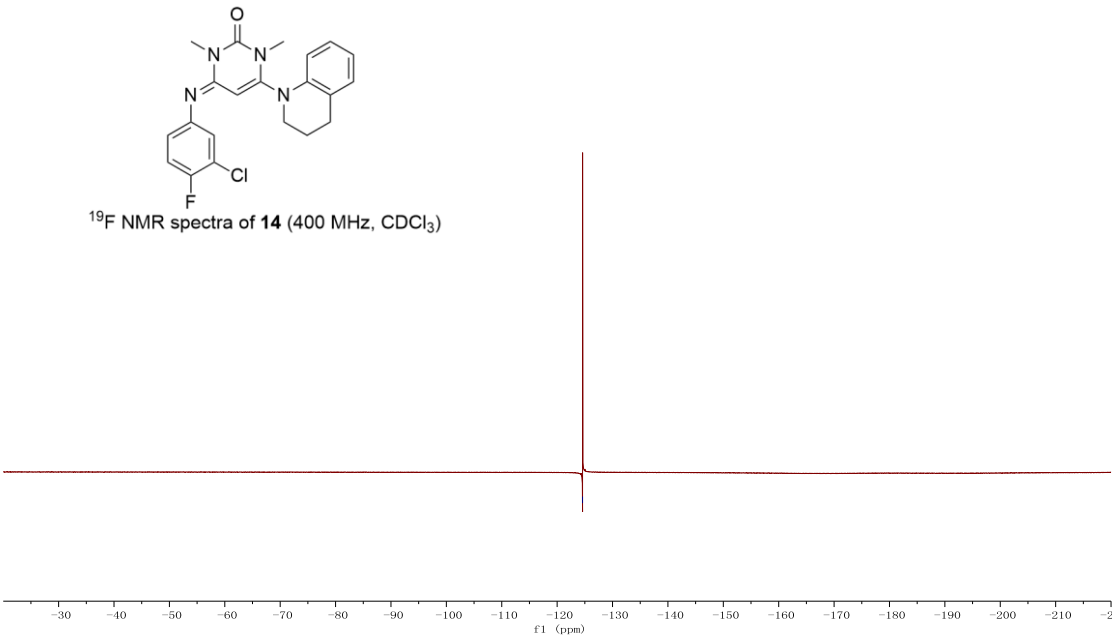


^{1}H NMR spectra of **14** (400 MHz, $CDCl_3$)

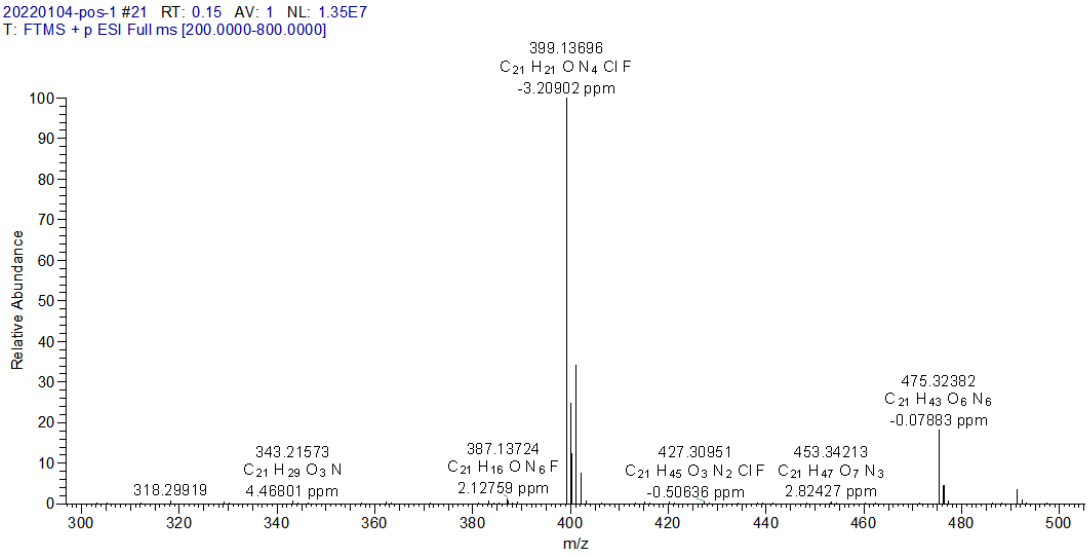


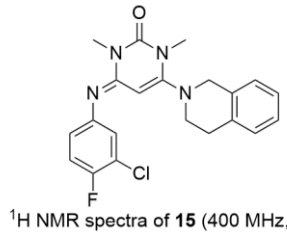


^{13}C {HNMR} spectra of **14** (101 MHz, $CDCl_3$)

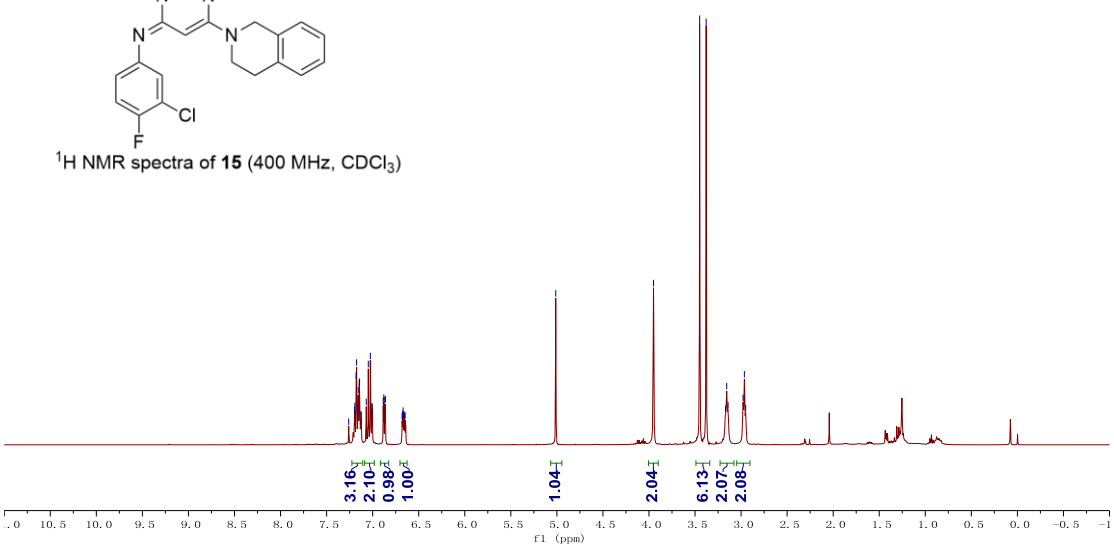


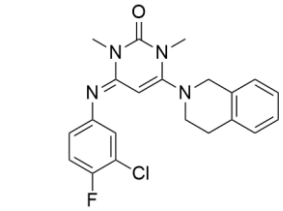
^{19}F NMR spectra of **14** (400 MHz, $CDCl_3$)



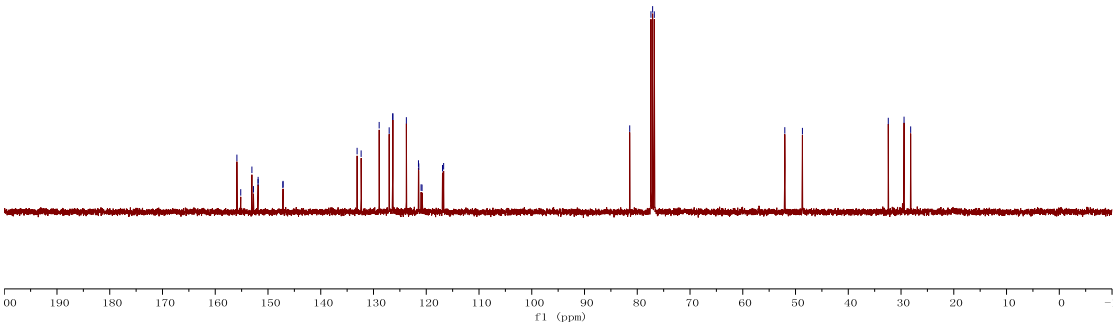


^{1}H NMR spectra of **15** (400 MHz, $CDCl_3$)

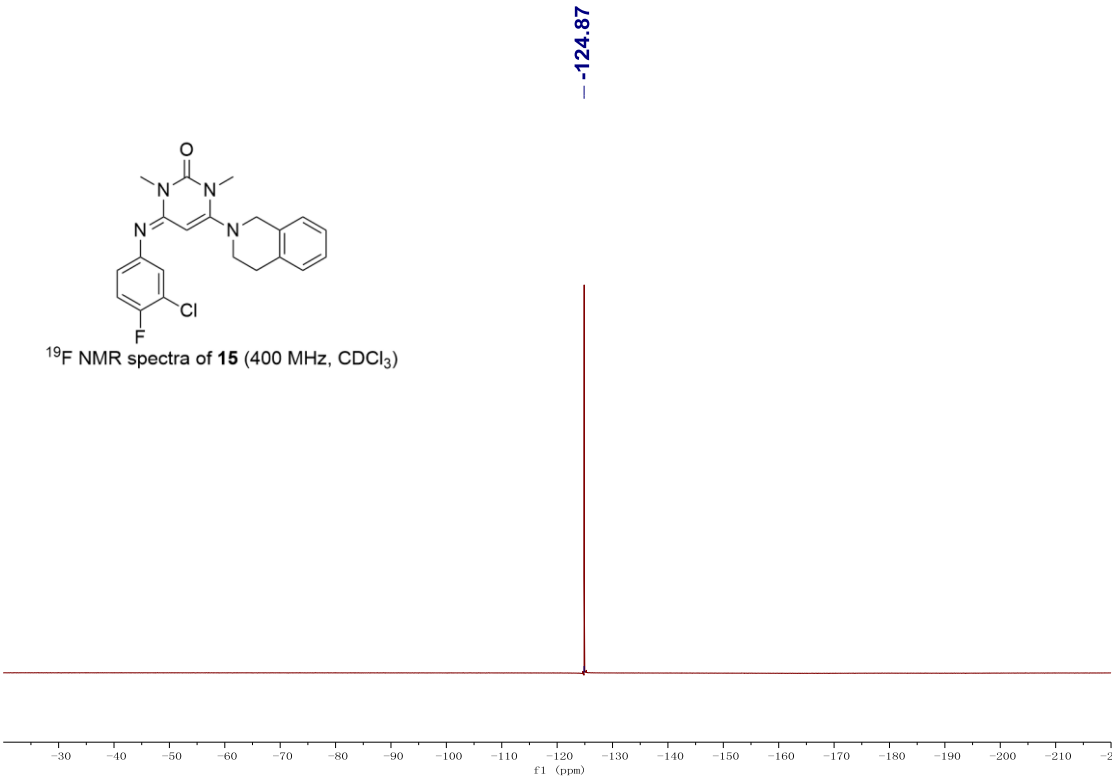


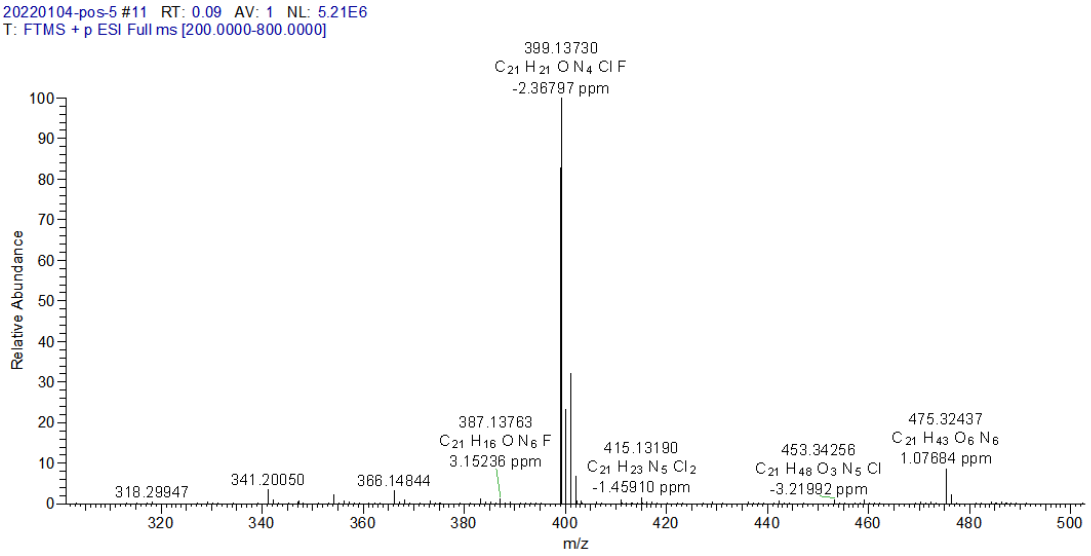


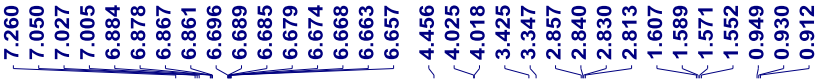
^{13}C {HNMR} spectra of **15** (101 MHz, $CDCl_3$)

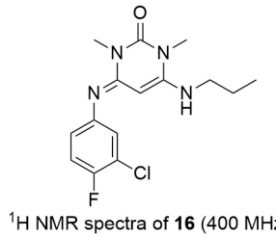


^{19}F NMR spectra of **15** (400 MHz, $CDCl_3$)

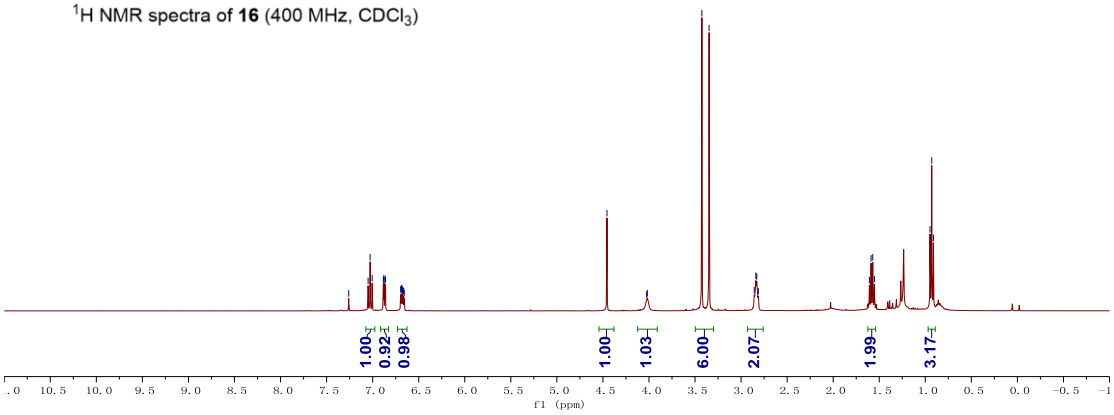


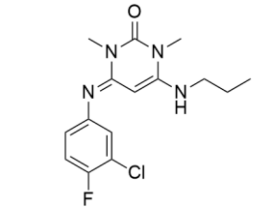




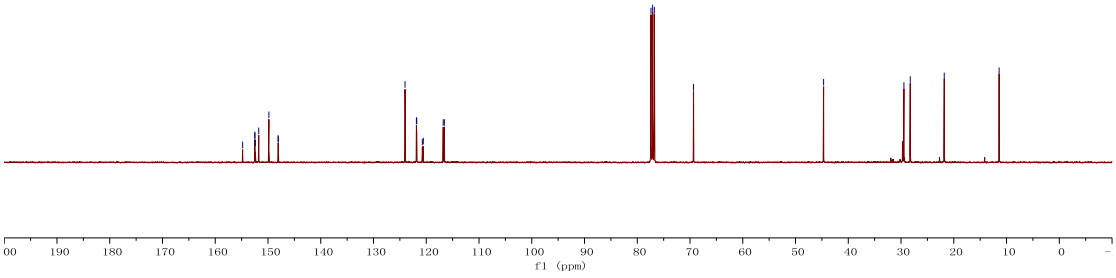


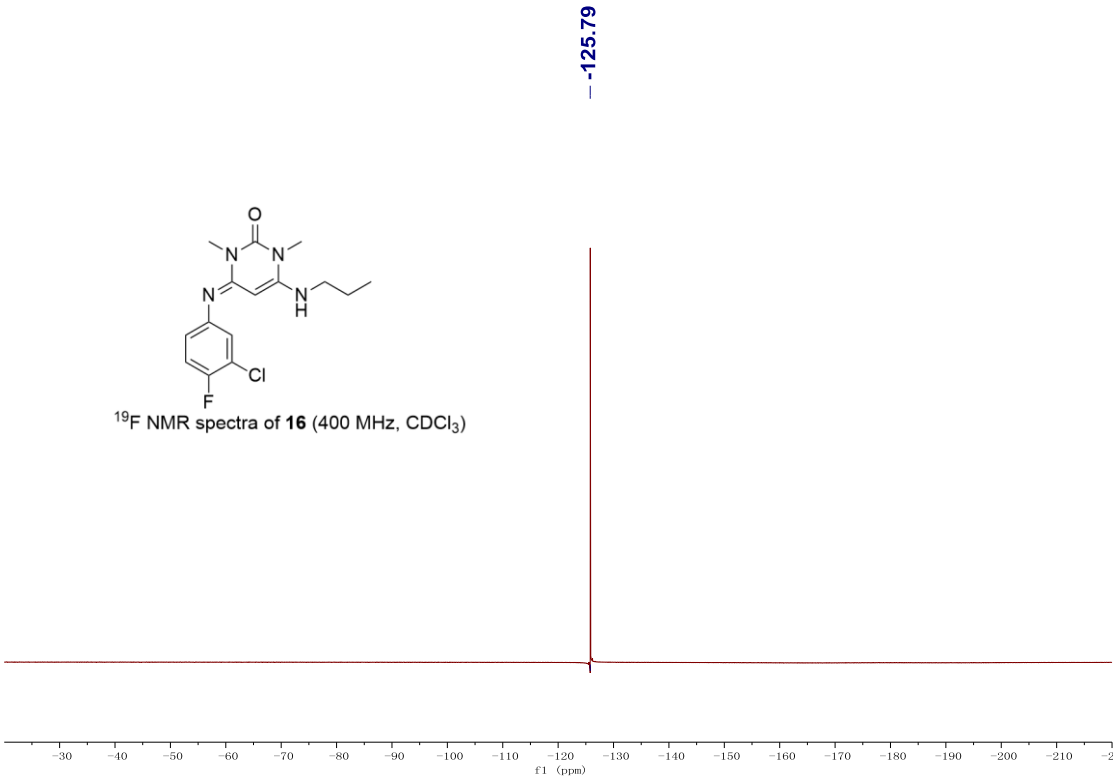
^{1}H NMR spectra of **16** (400 MHz, $CDCl_3$)





^{13}C {HNMR} spectra of **16** (101 MHz, $CDCl_3$)

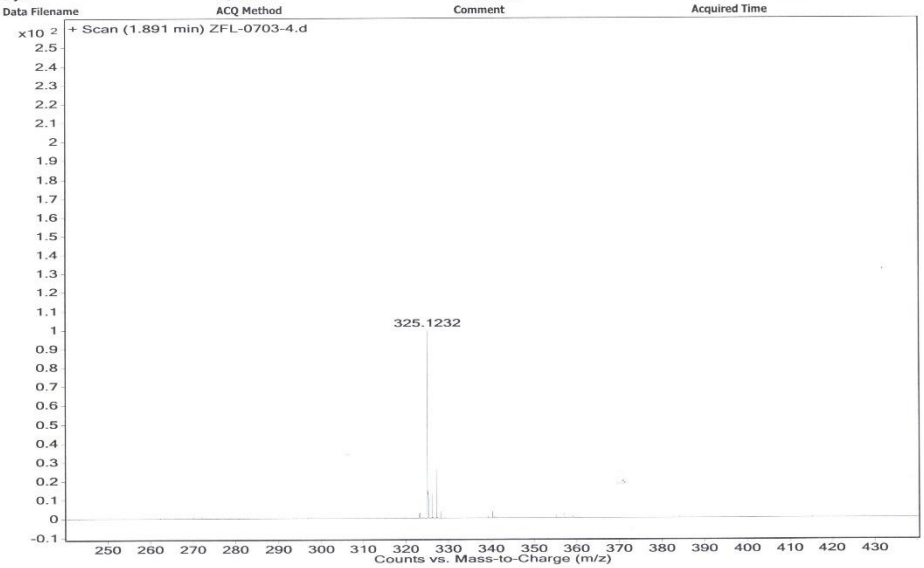


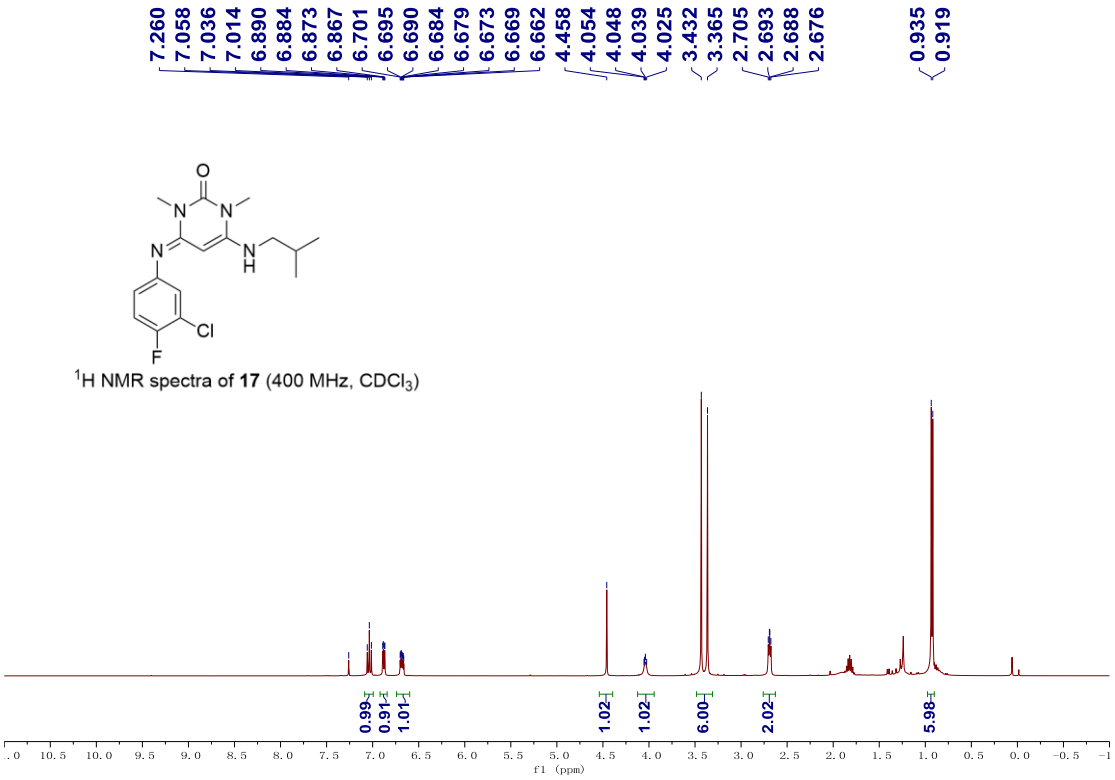


^{19}F NMR spectra of **16** (400 MHz, $CDCl_3$)

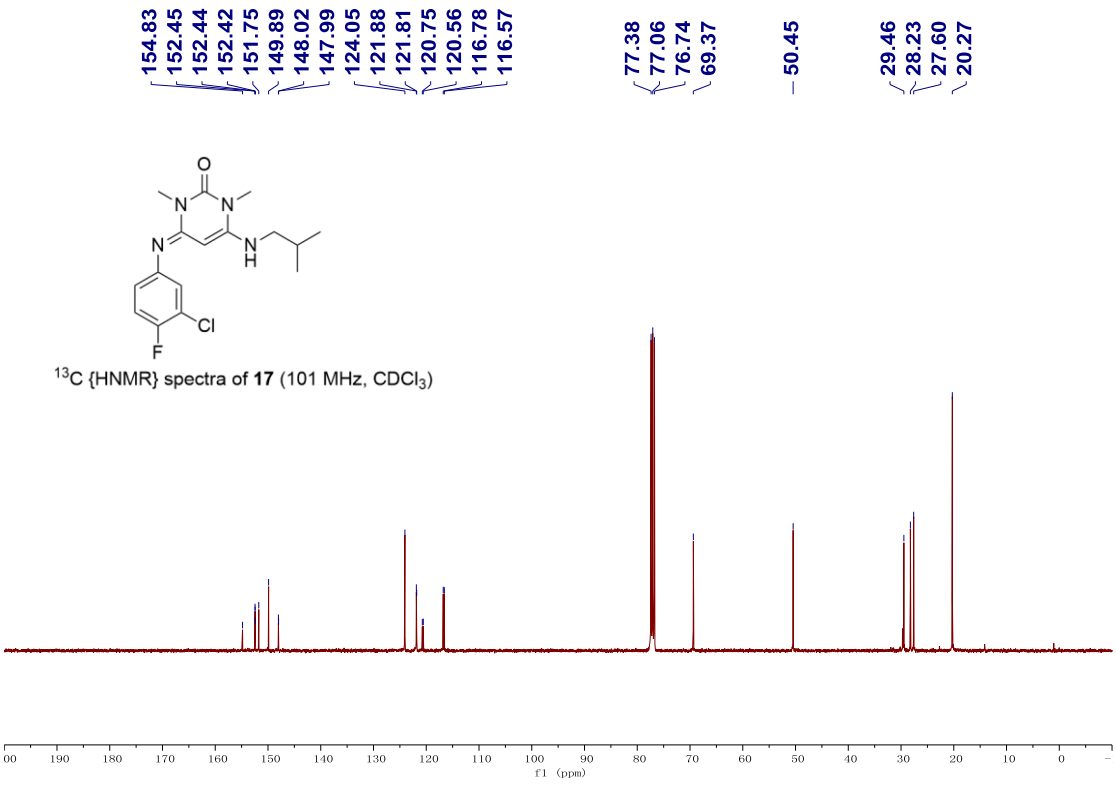
2.

Sample Name	Position	Instrument Name	User Name
Inj Vol	InjPosition	SampleType	IRM Calibration Status
Data Filename	ACQ Method	Comment	Acquired Time

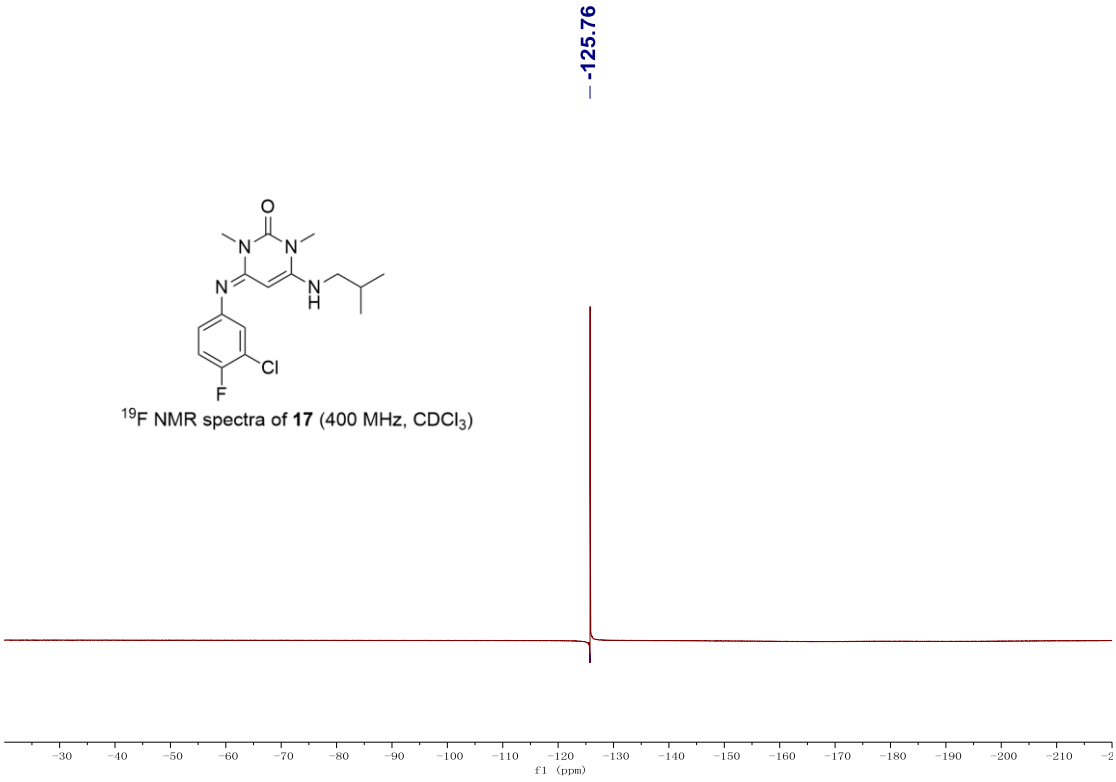




^{1}H NMR spectra of **17** (400 MHz, $CDCl_3$)



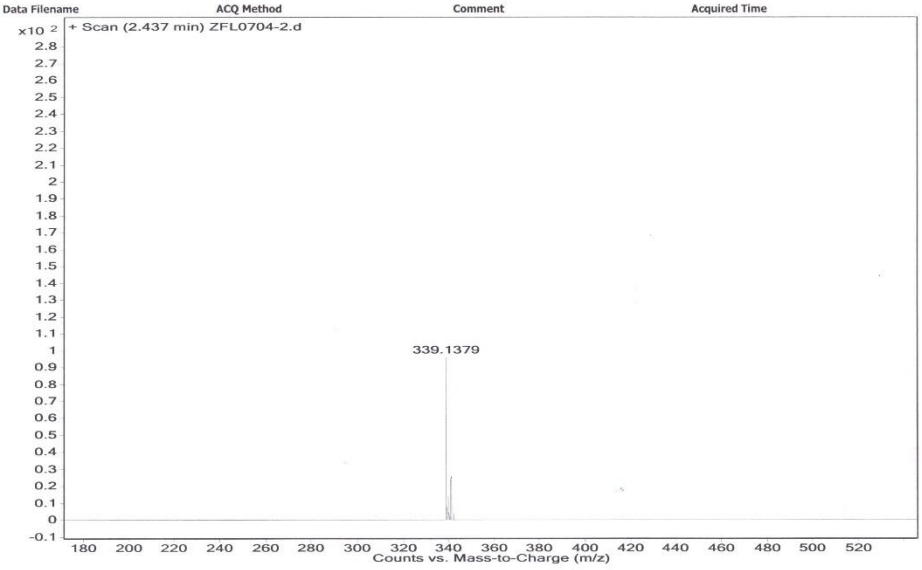
^{13}C {HNMR} spectra of **17** (101 MHz, $CDCl_3$)

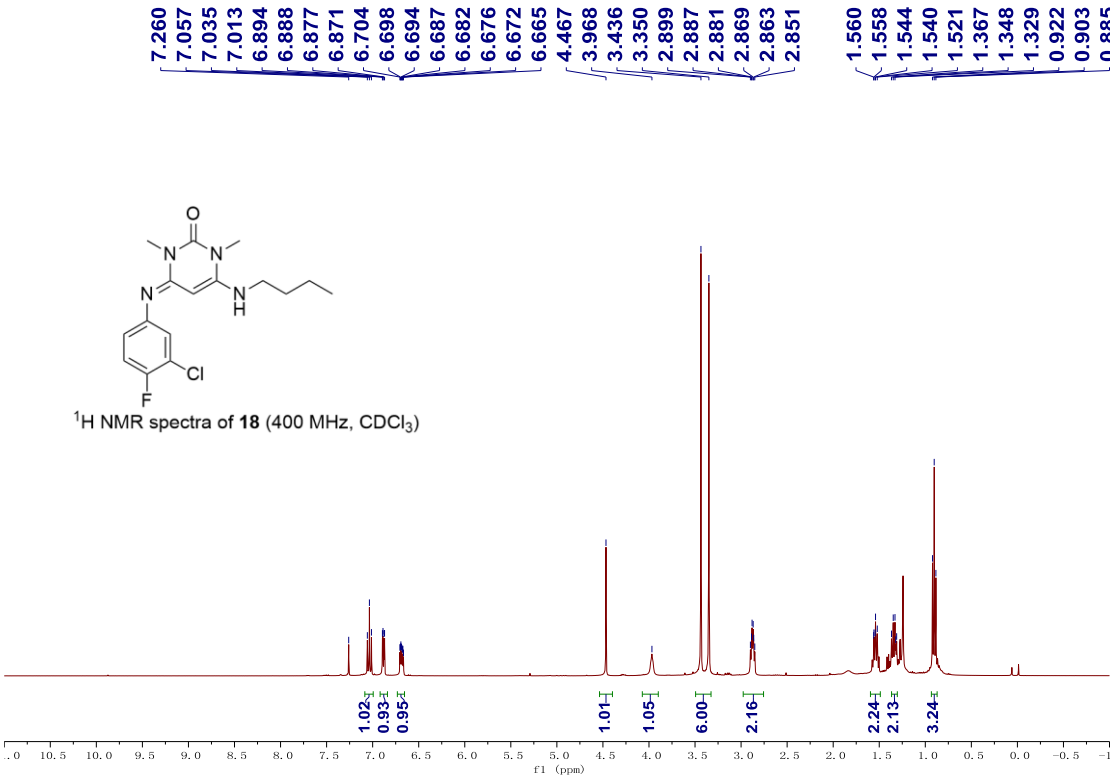


^{19}F NMR spectra of **17** (400 MHz, $CDCl_3$)

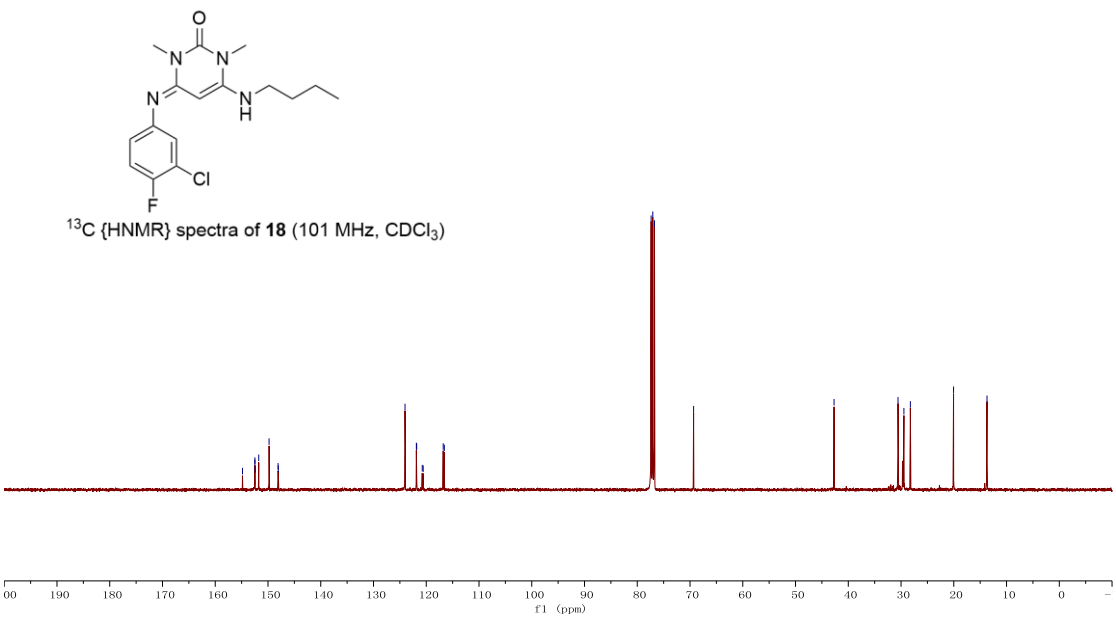
10.

Sample Name	Position	Instrument Name	User Name
Inj Vol	InjPosition	SampleType	IRM Calibration Status
Data Filename	ACQ Method	Comment	Acquired Time



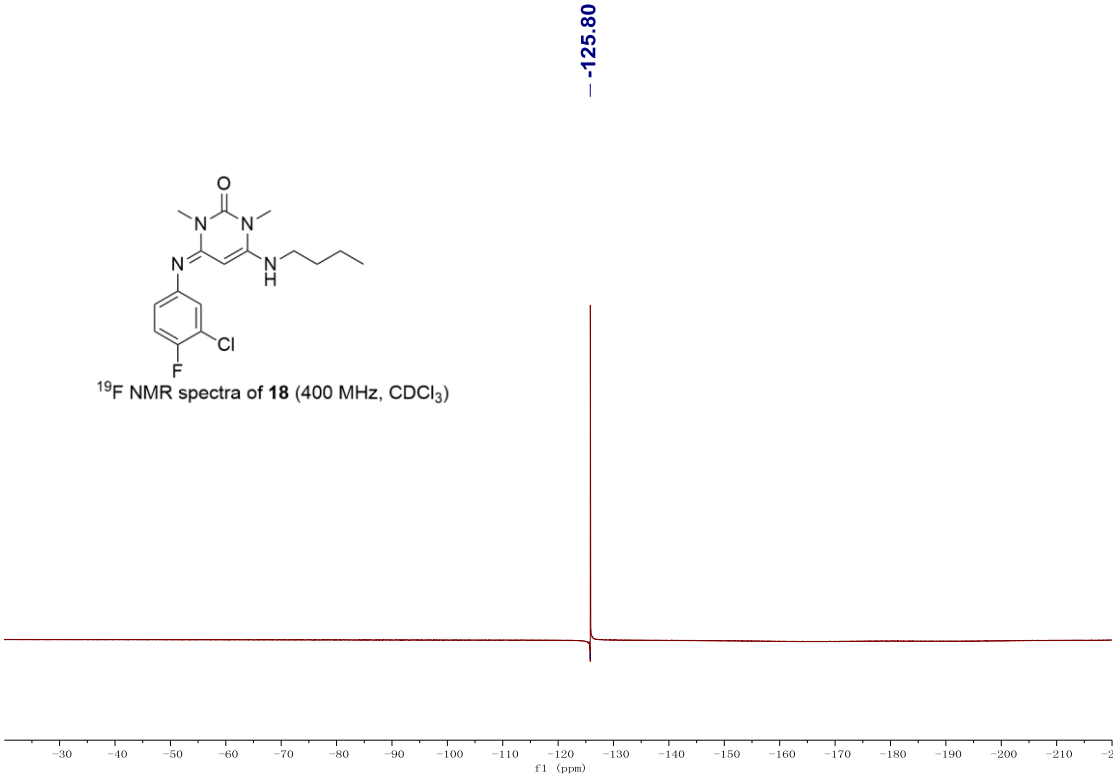


^{1}H NMR spectra of **18** (400 MHz, $CDCl_3$)



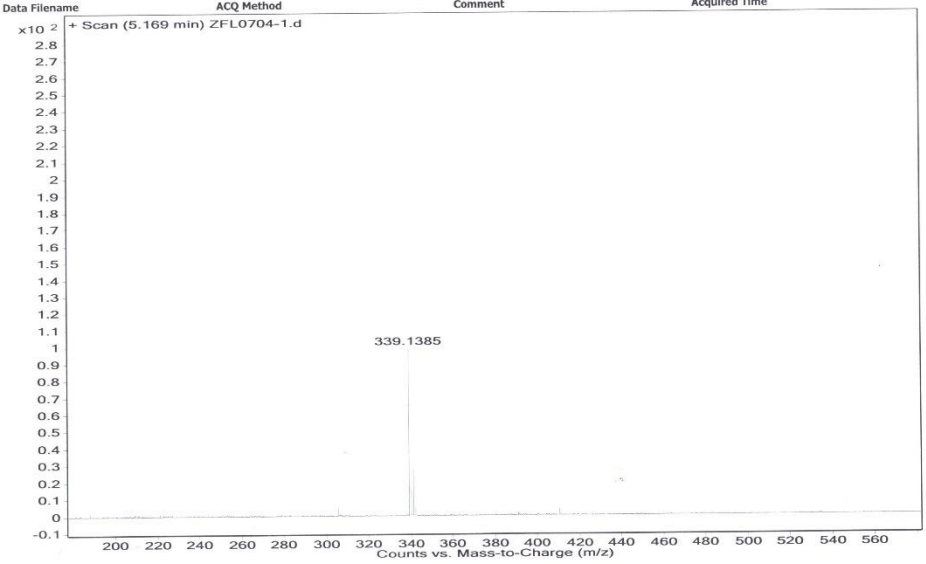
^{13}C {HNMR} spectra of **18** (101 MHz, $CDCl_3$)

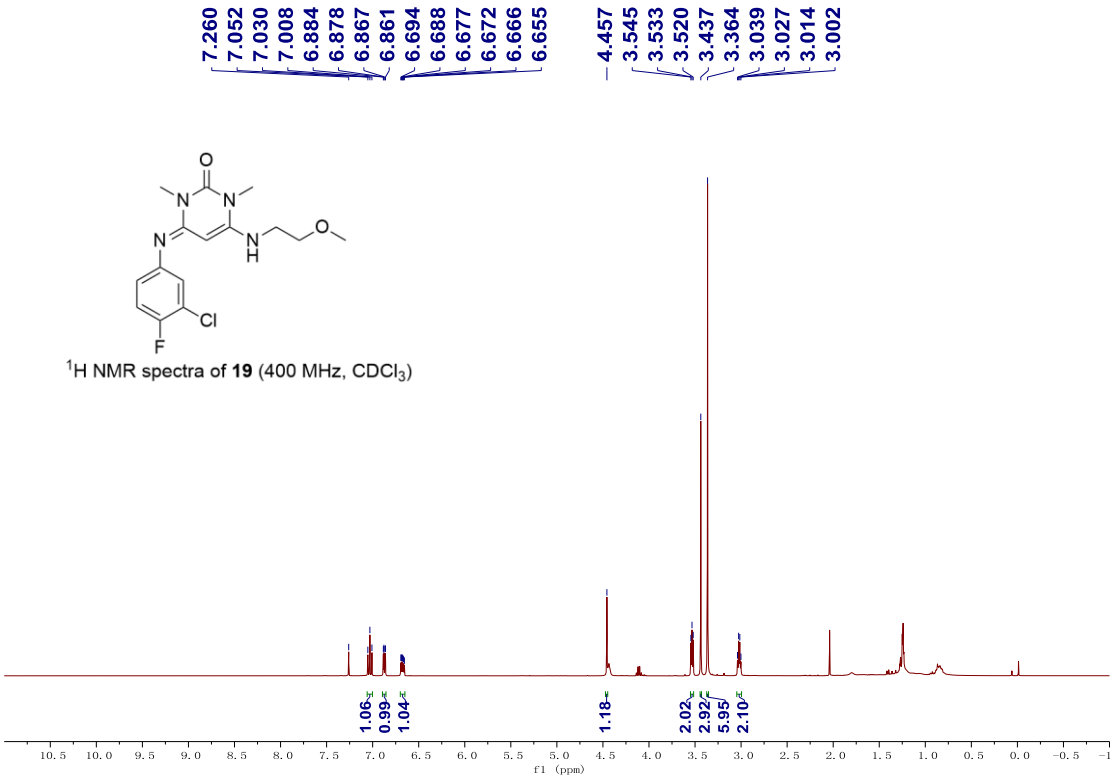
^{19}F NMR spectra of **18** (400 MHz, $CDCl_3$)



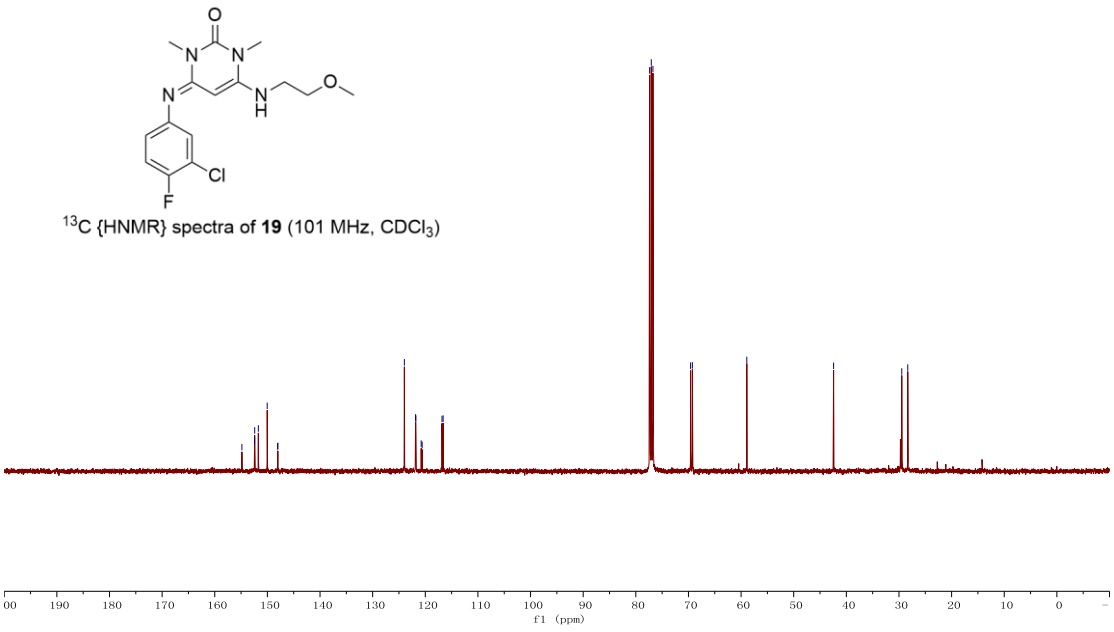
9.

Sample Name	Position	Instrument Name	User Name
Inj Vol	InjPosition	SampleType	IRM Calibration Status
Data Filename	ACQ Method	Comment	Acquired Time



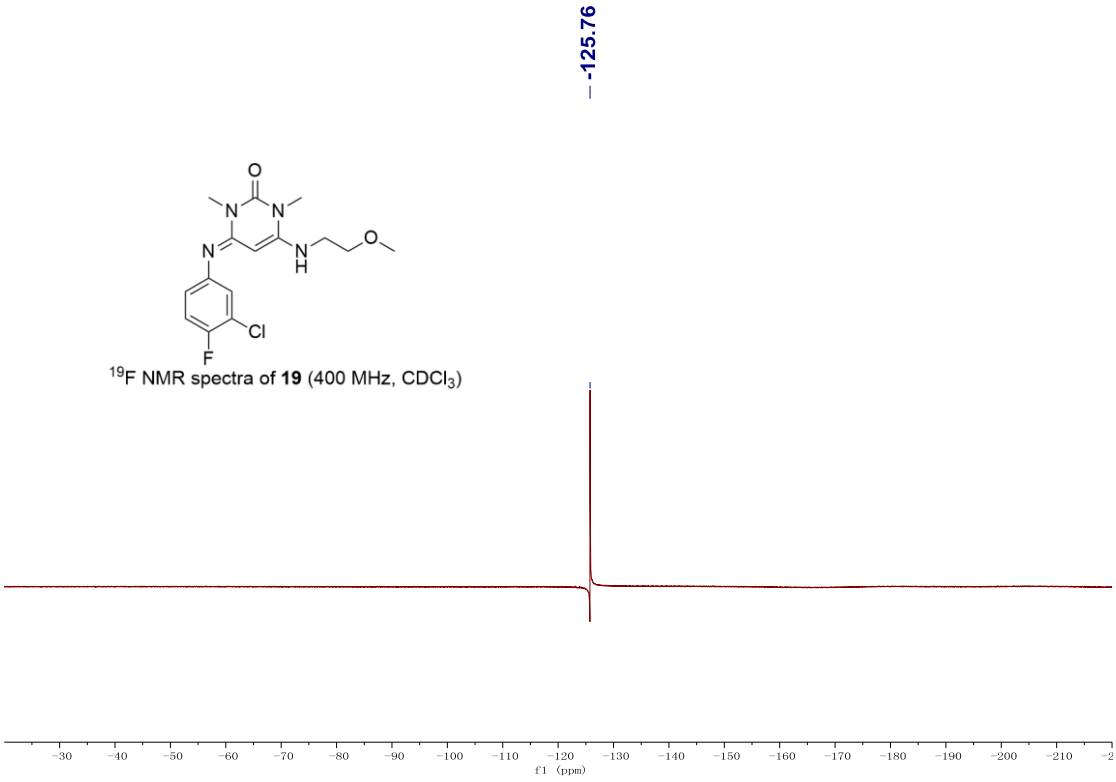


^{1}H NMR spectra of **19** (400 MHz, $CDCl_3$)



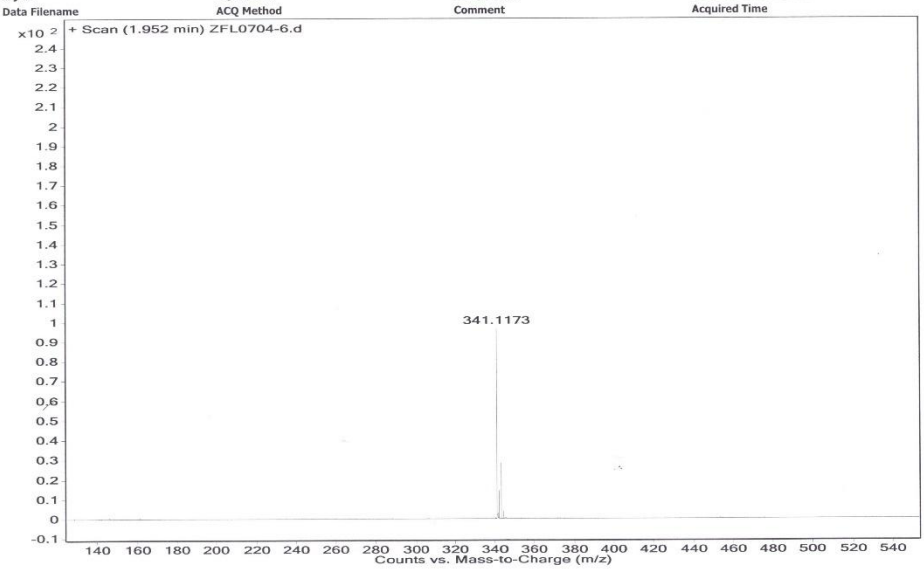
^{13}C {HNMR} spectra of **19** (101 MHz, $CDCl_3$)

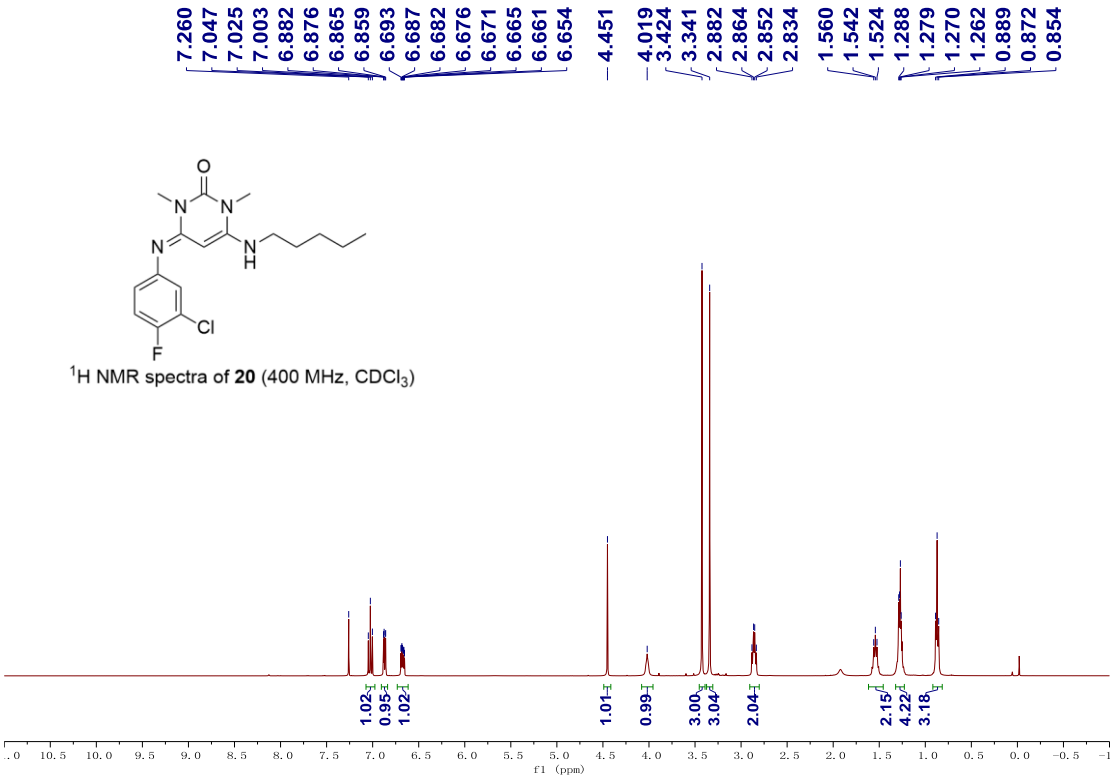
^{19}F NMR spectra of **19** (400 MHz, $CDCl_3$)



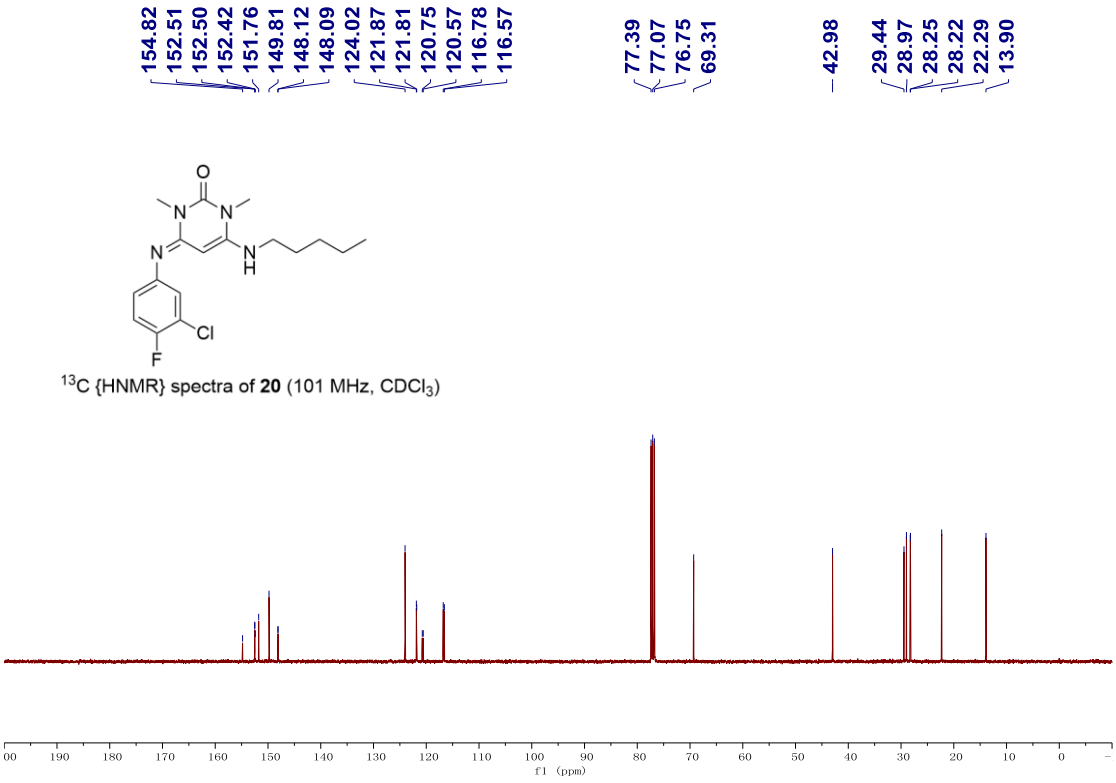
17.

Sample Name	Position	Instrument Name	User Name
Inj Vol	InjPosition	SampleType	IRM Calibration Status
Data Filename	ACQ Method	Comment	Acquired Time

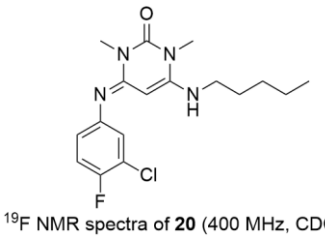




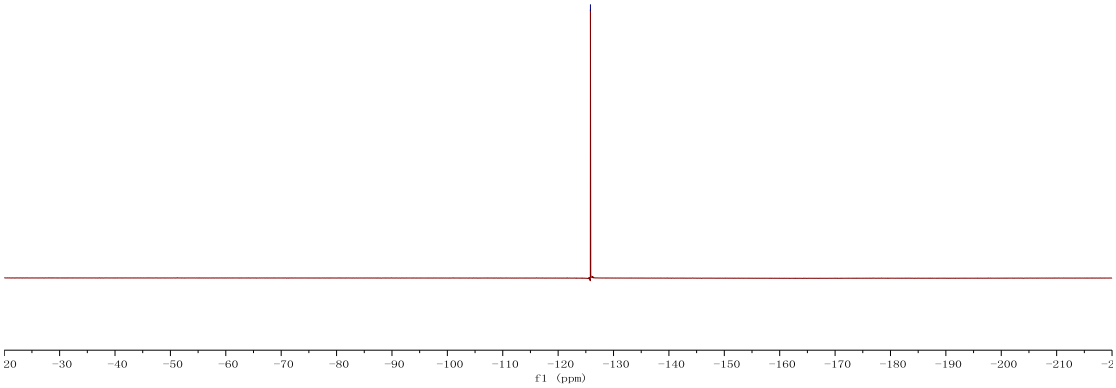
^{1}H NMR spectra of **20** (400 MHz, $CDCl_3$)



^{13}C {HNMR} spectra of **20** (101 MHz, $CDCl_3$)

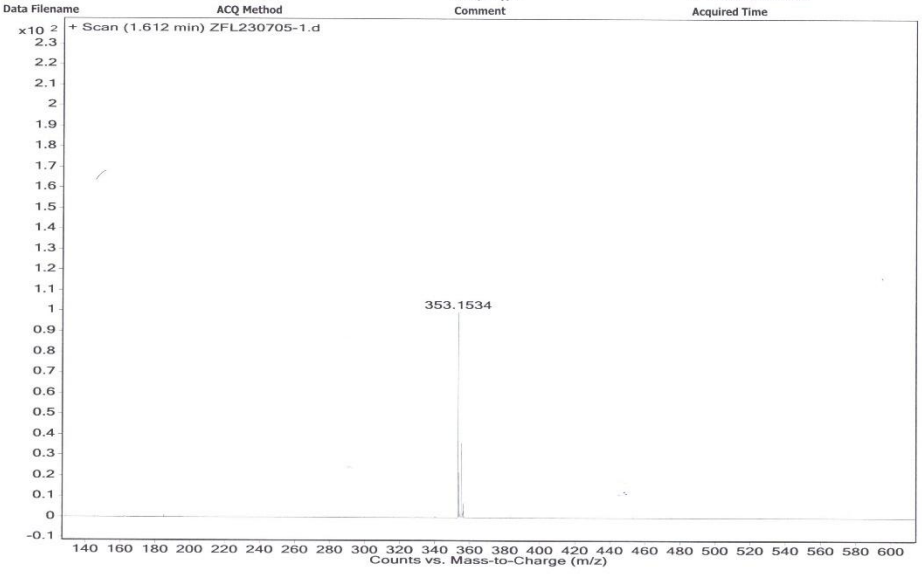


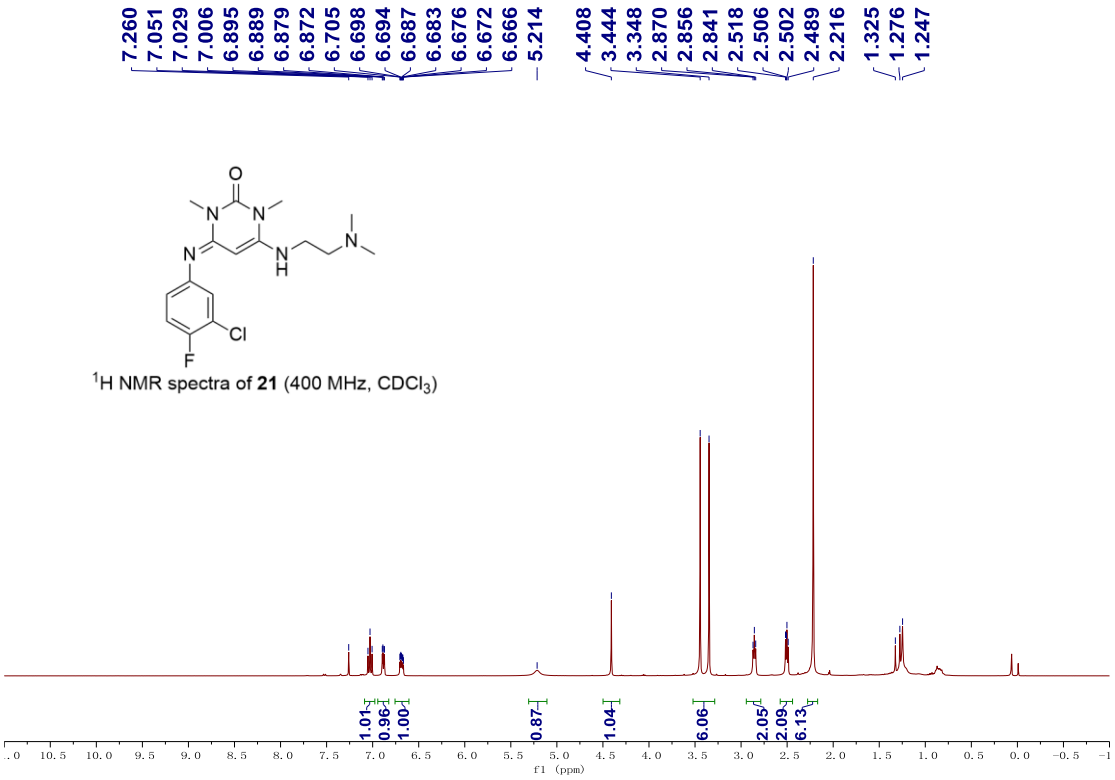
^{19}F NMR spectra of **20** (400 MHz, $CDCl_3$)



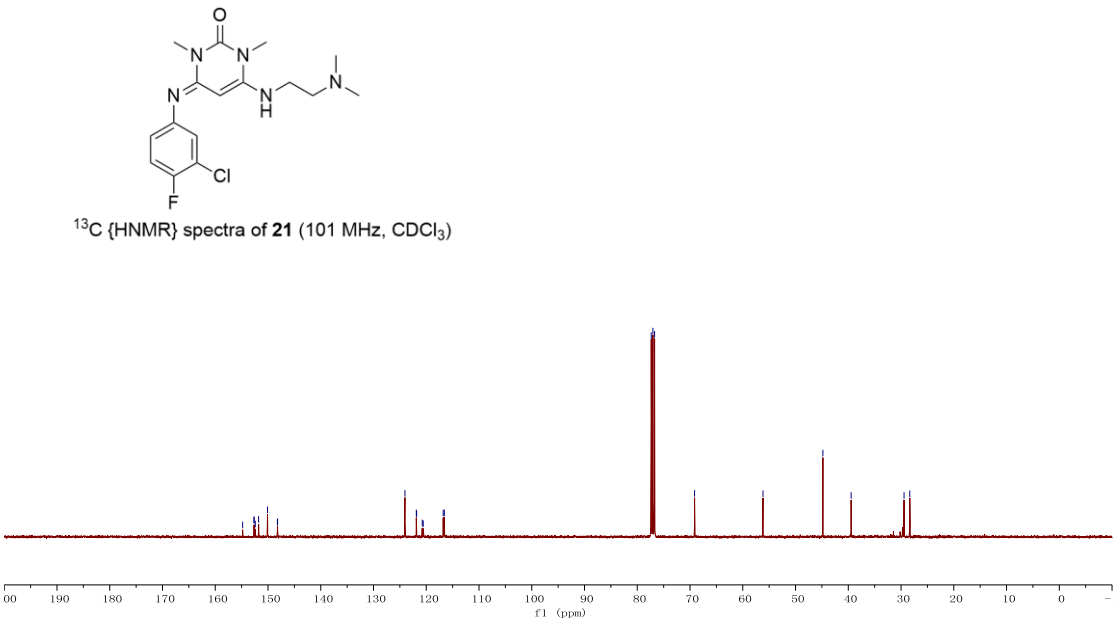
21.

Sample Name	Position	Instrument Name	User Name
Inj Vol	InjPosition	SampleType	IRM Calibration Status
Data Filename	ACQ Method	Comment	Acquired Time



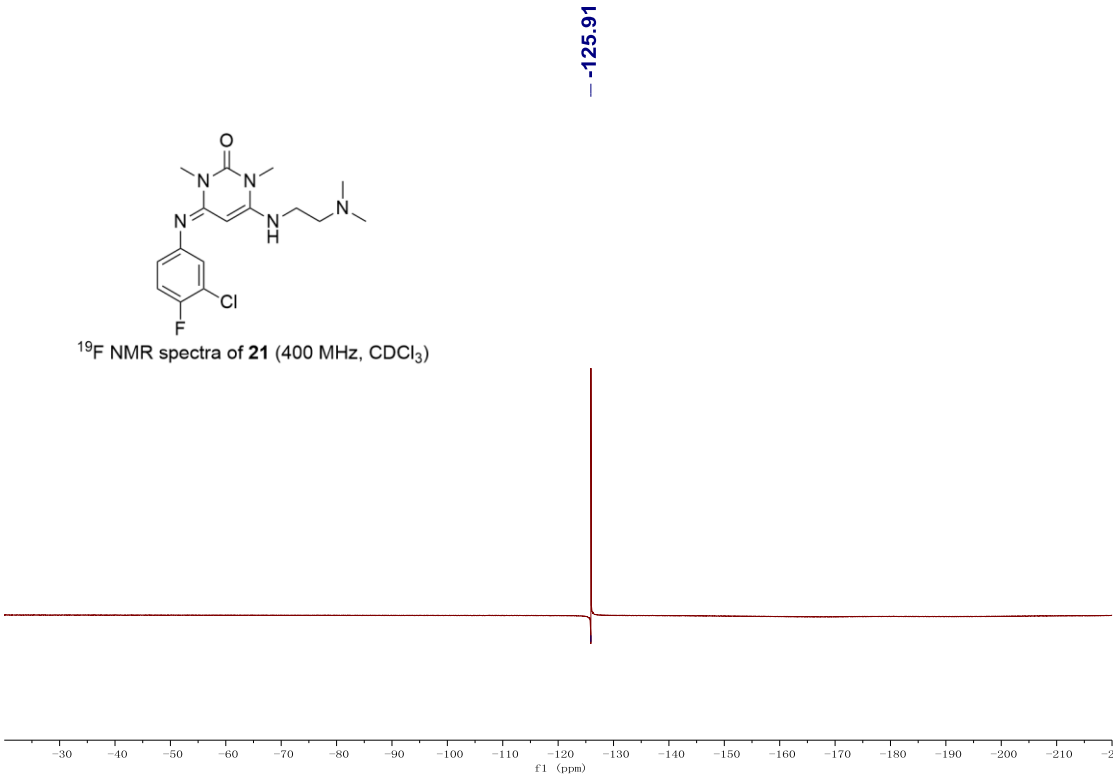


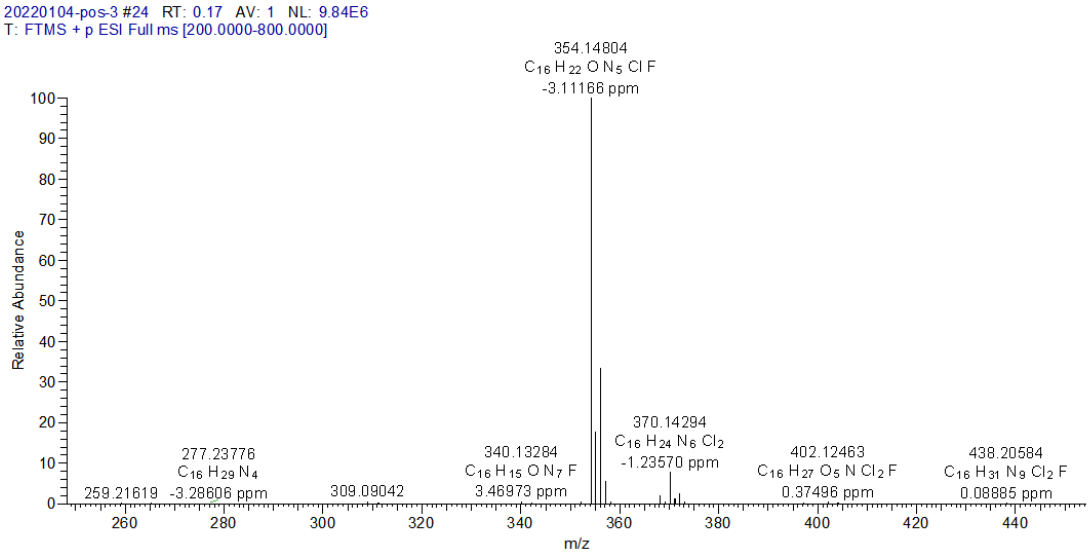
^{1}H NMR spectra of **21** (400 MHz, $CDCl_3$)

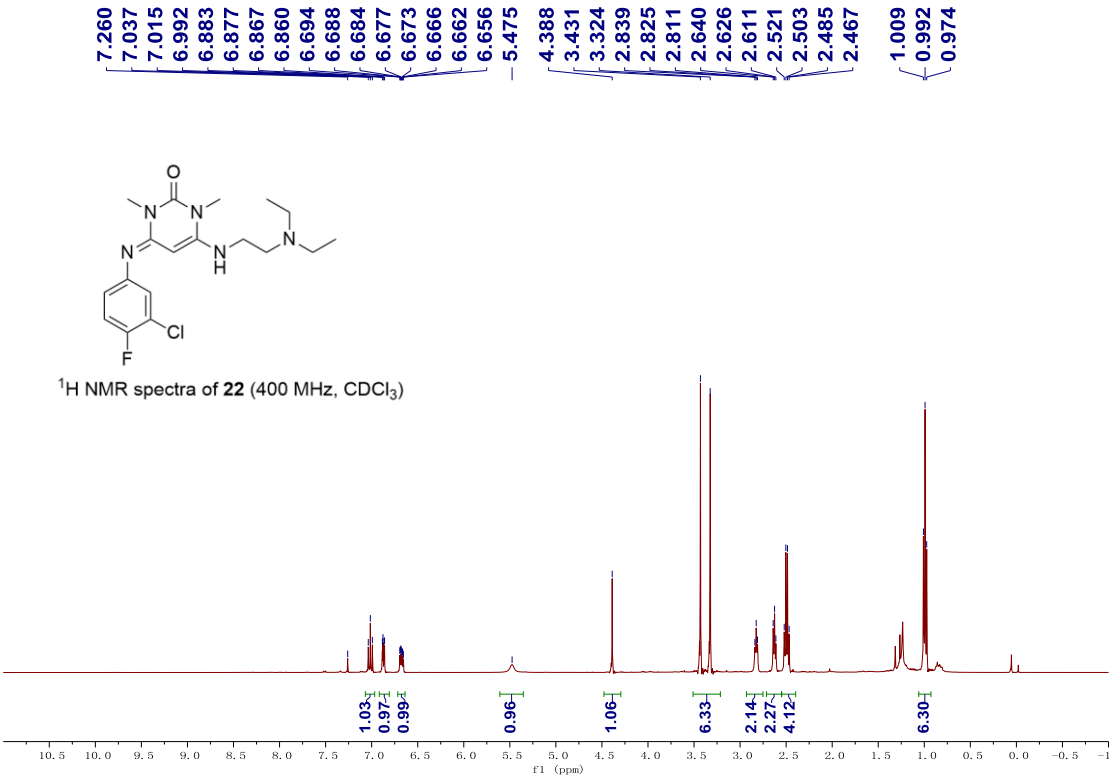


^{13}C {HNMR} spectra of **21** (101 MHz, $CDCl_3$)

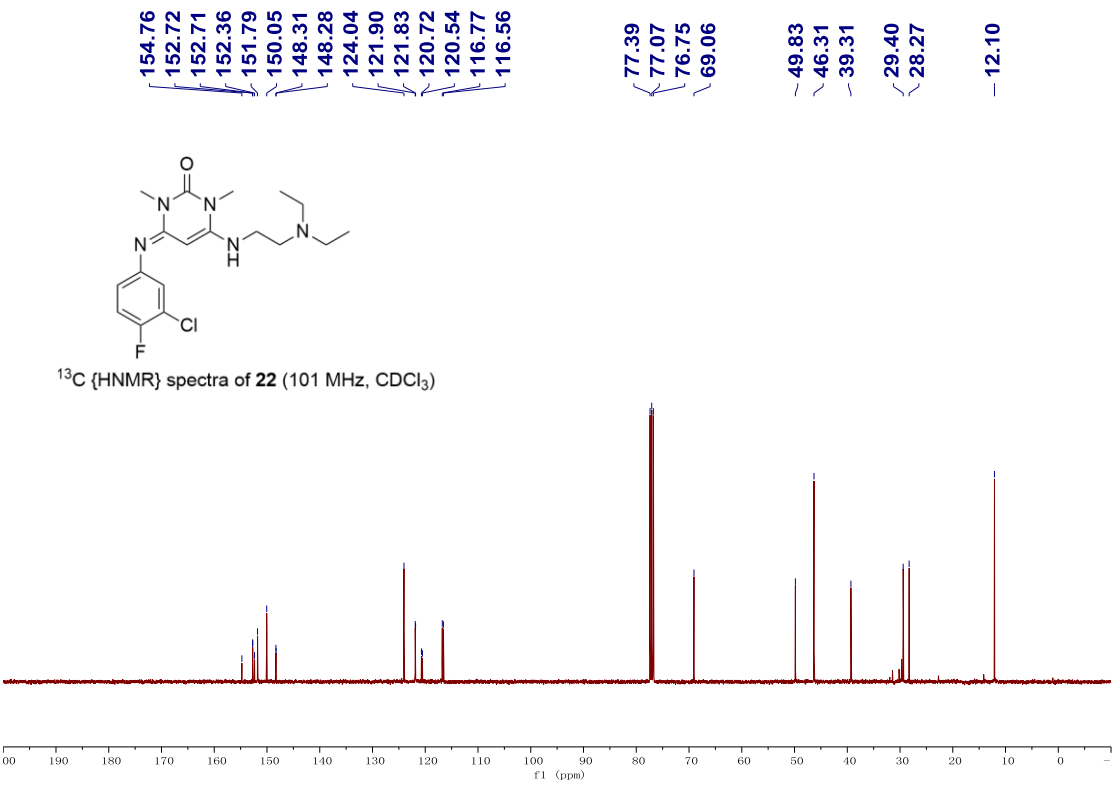
^{19}F NMR spectra of **21** (400 MHz, $CDCl_3$)



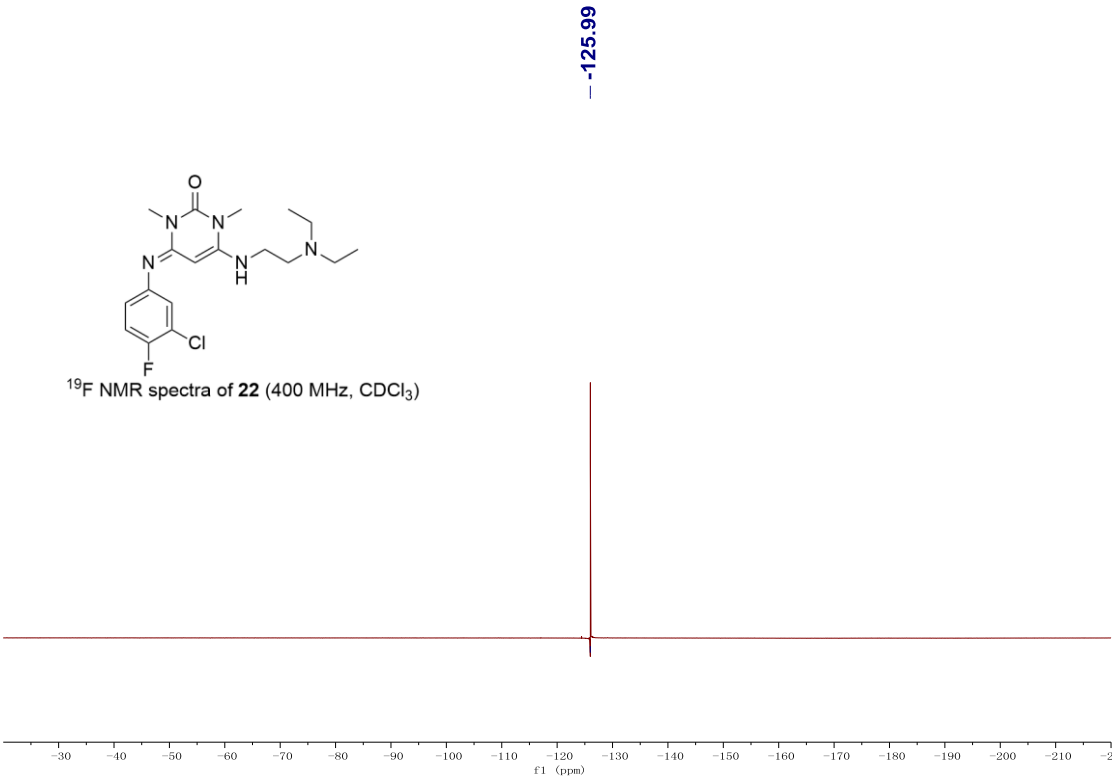




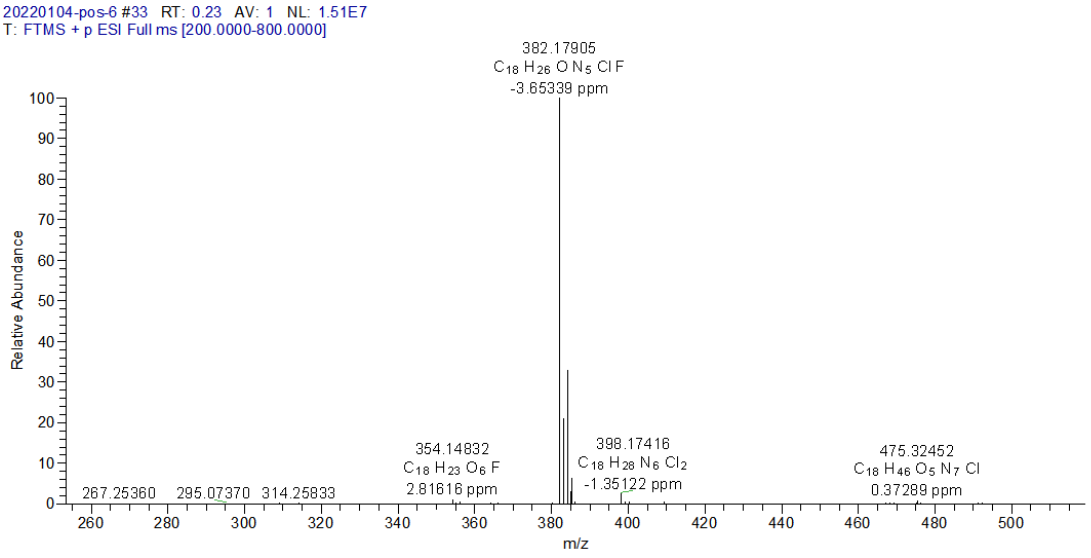
^{1}H NMR spectra of **22** (400 MHz, $CDCl_3$)

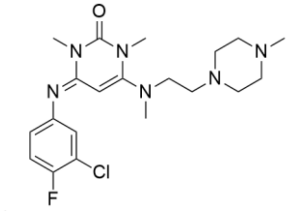


^{13}C {HNMR} spectra of **22** (101 MHz, $CDCl_3$)

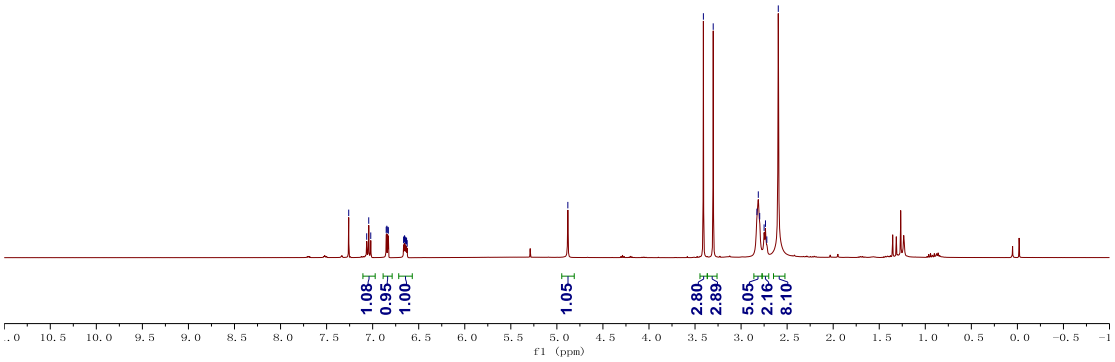


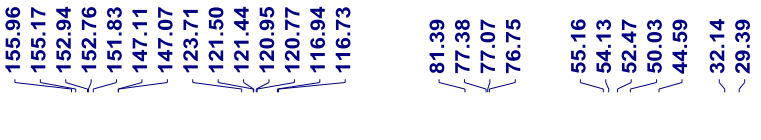
^{19}F NMR spectra of **22** (400 MHz, $CDCl_3$)



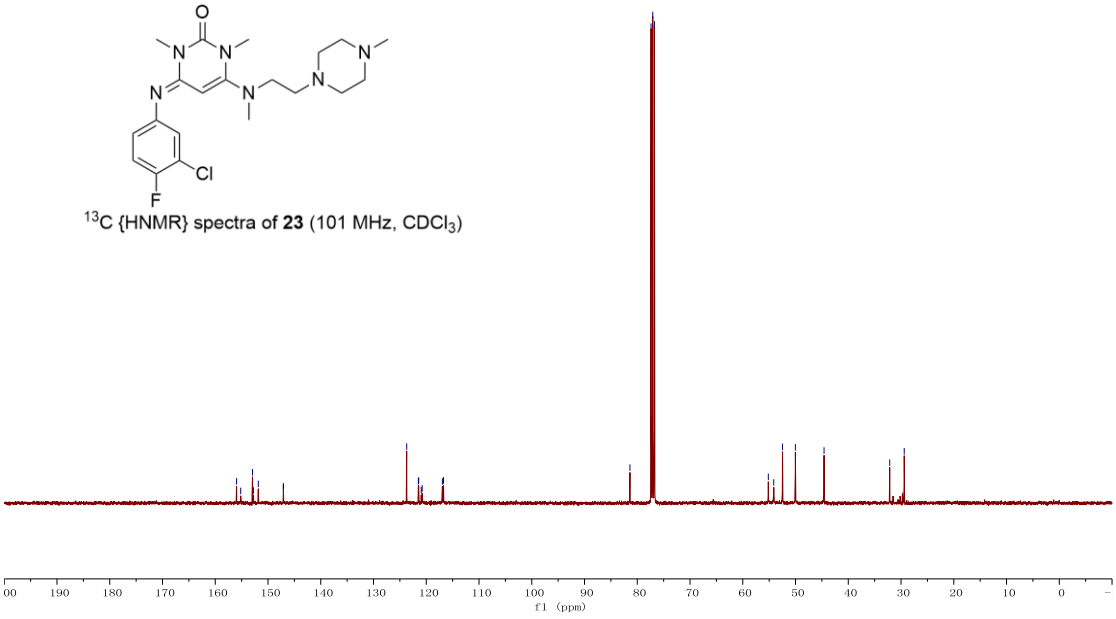


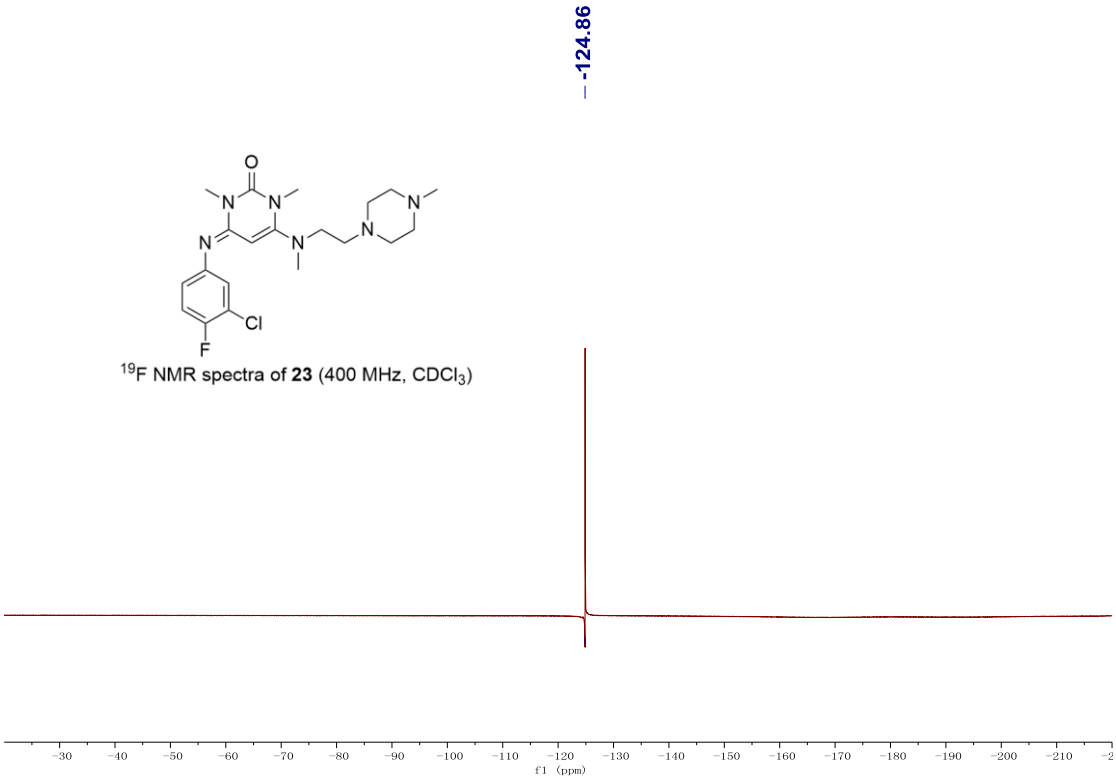
^{1}H NMR spectra of **23** (400 MHz, $CDCl_3$)





^{13}C {HNMR} spectra of **23** (101 MHz, $CDCl_3$)

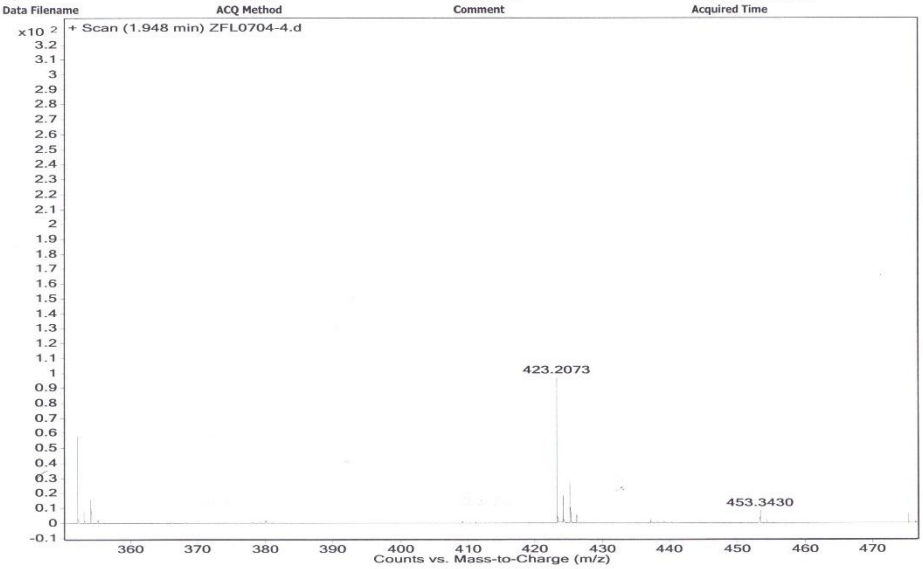


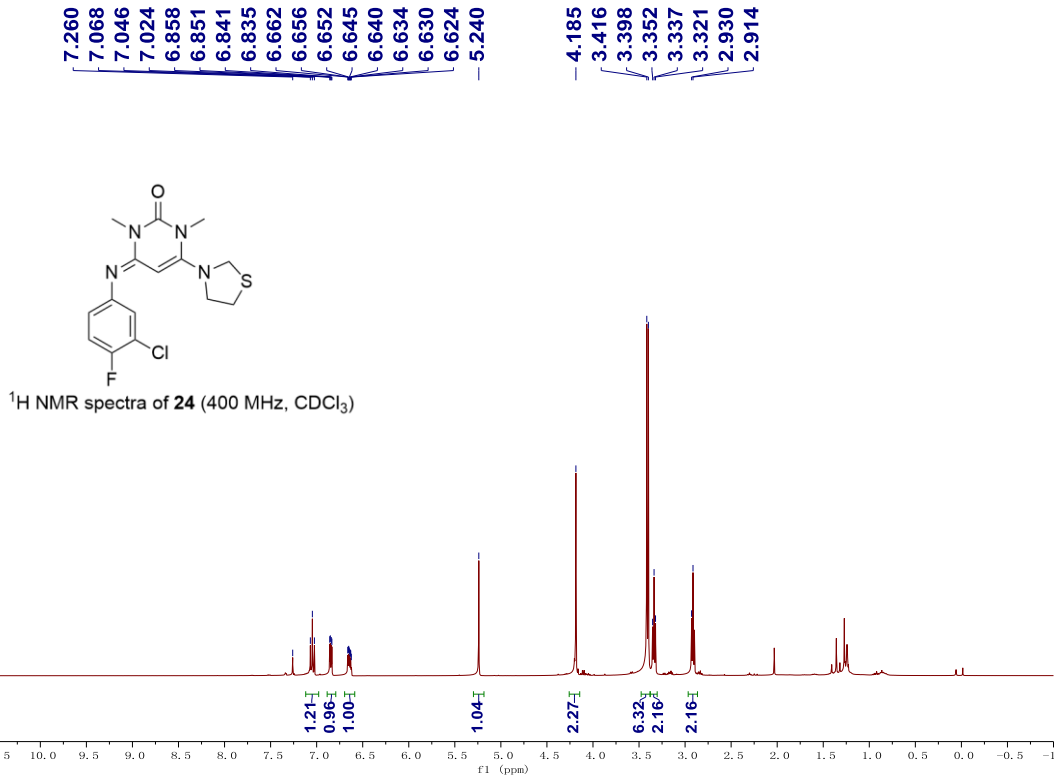


^{19}F NMR spectra of **23** (400 MHz, $CDCl_3$)

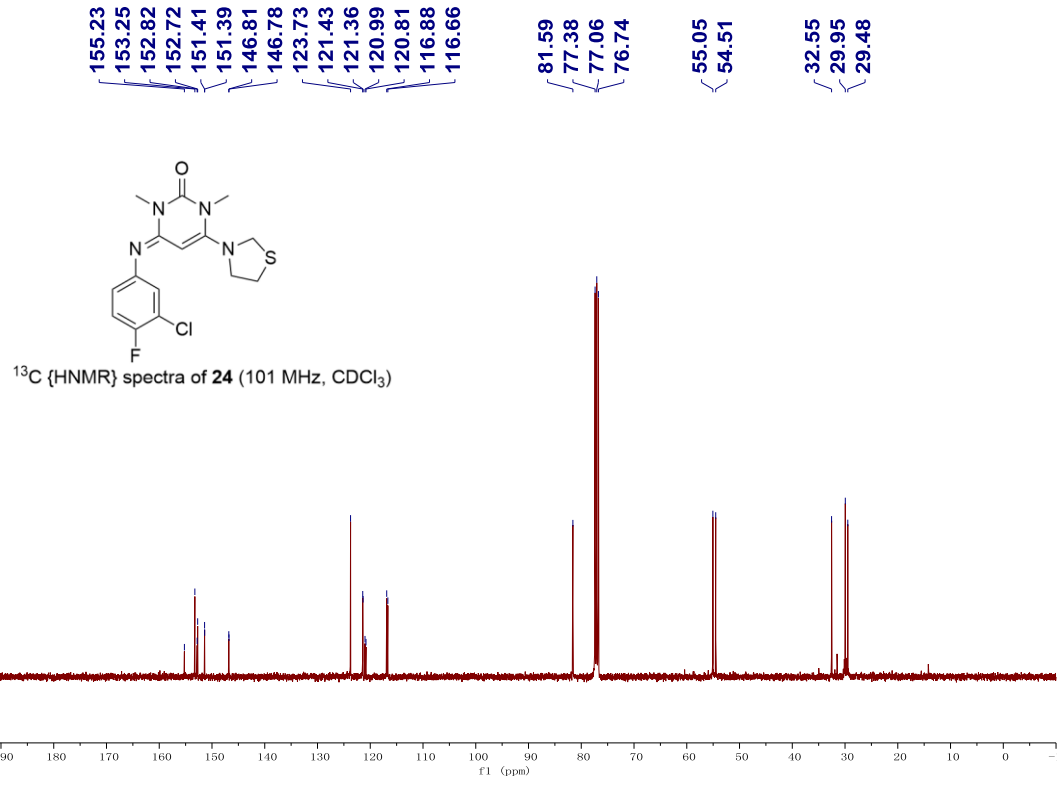
12.

Sample Name	Position	Instrument Name	User Name
Inj Vol	InjPosition	SampleType	IRM Calibration Status
Data Filename	ACQ Method	Comment	Acquired Time



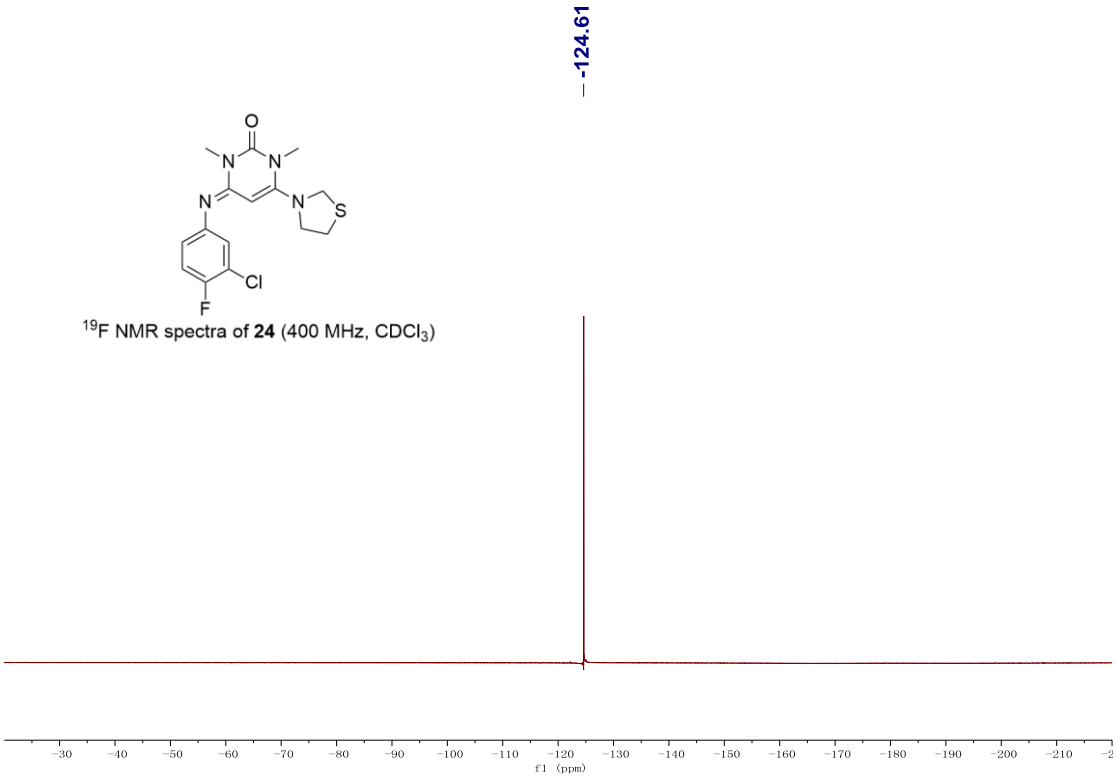


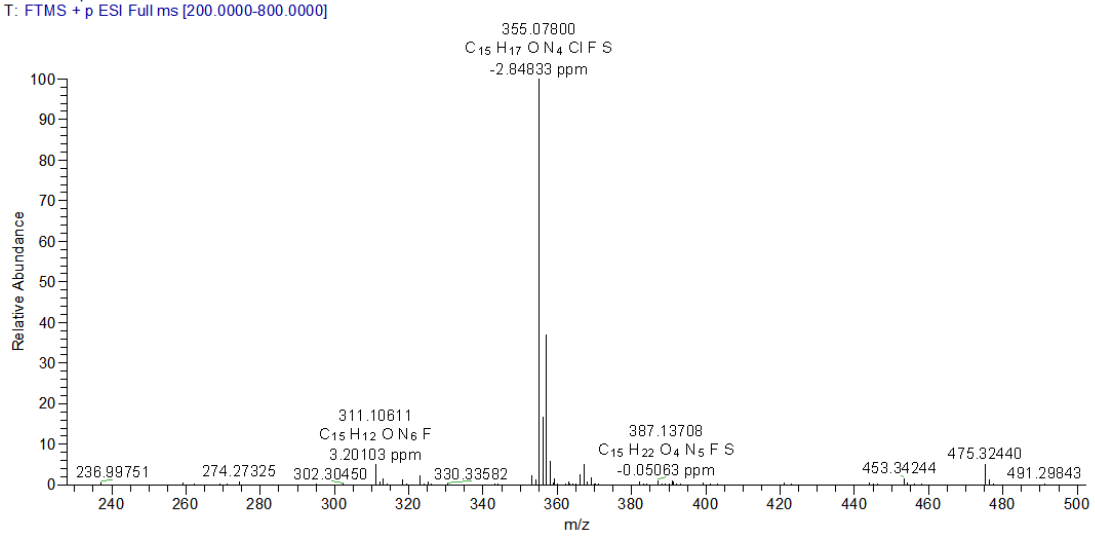
^{1}H NMR spectra of **24** (400 MHz, $CDCl_3$)

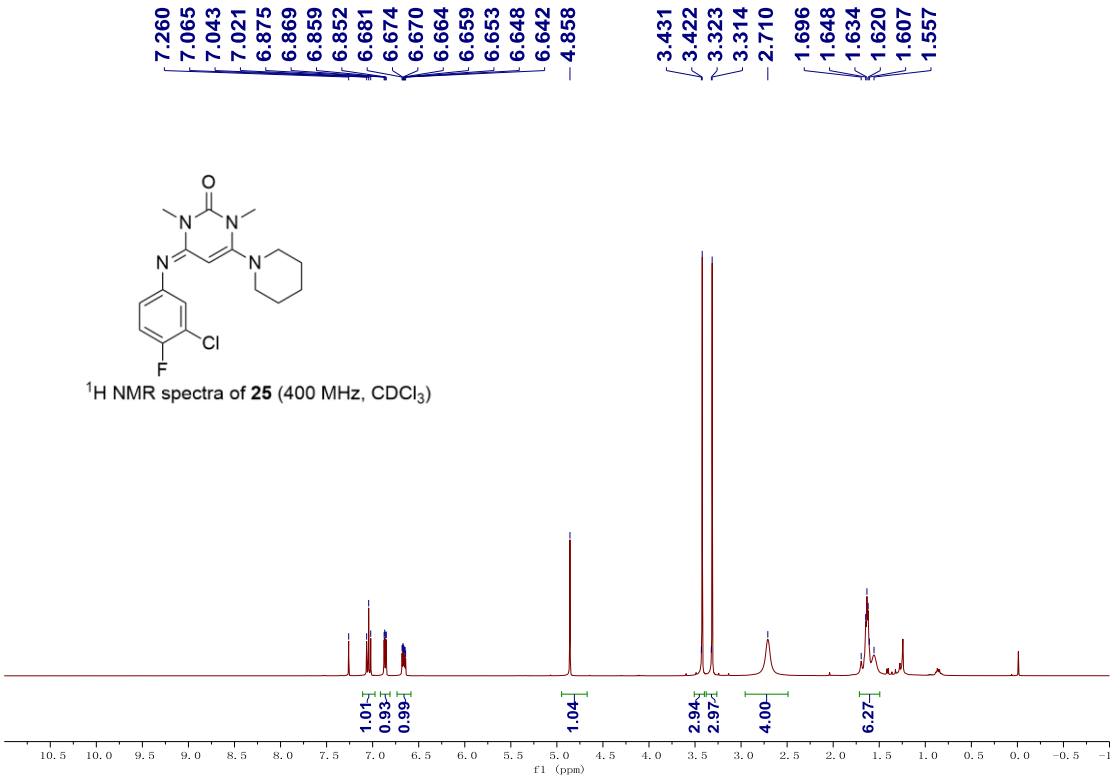


^{13}C {HNMR} spectra of **24** (101 MHz, $CDCl_3$)

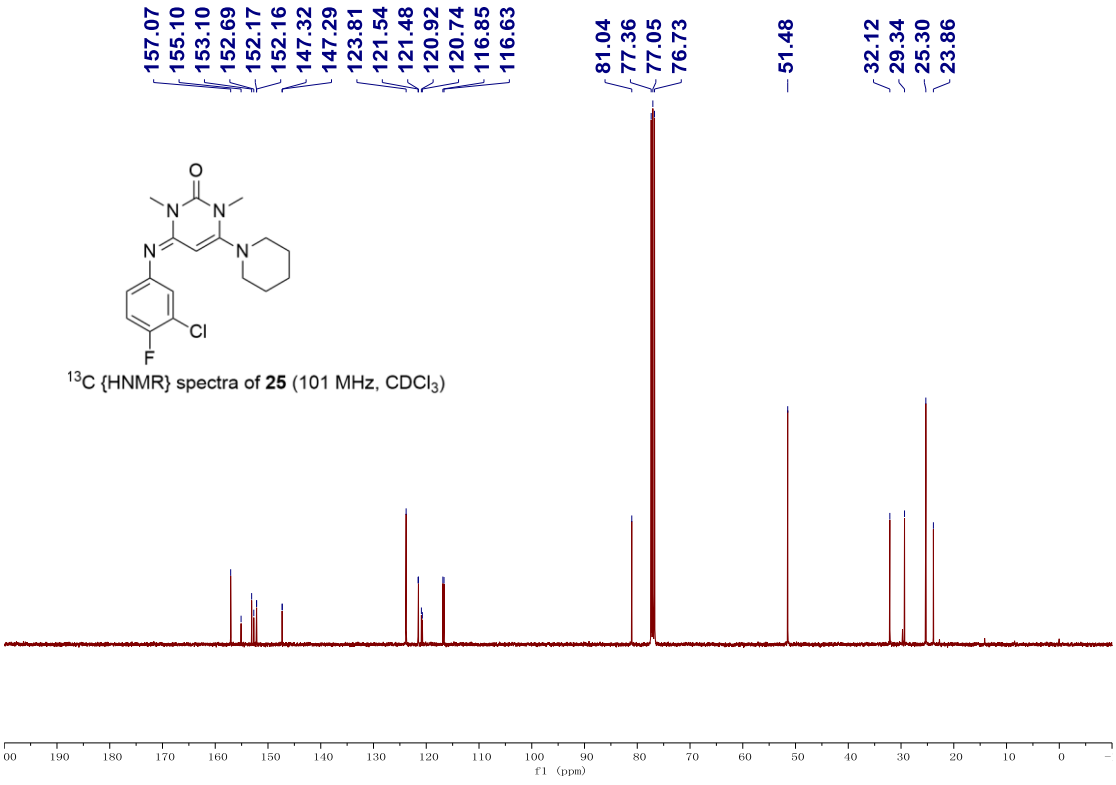
^{19}F NMR spectra of **24** (400 MHz, $CDCl_3$)



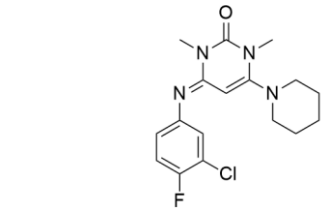




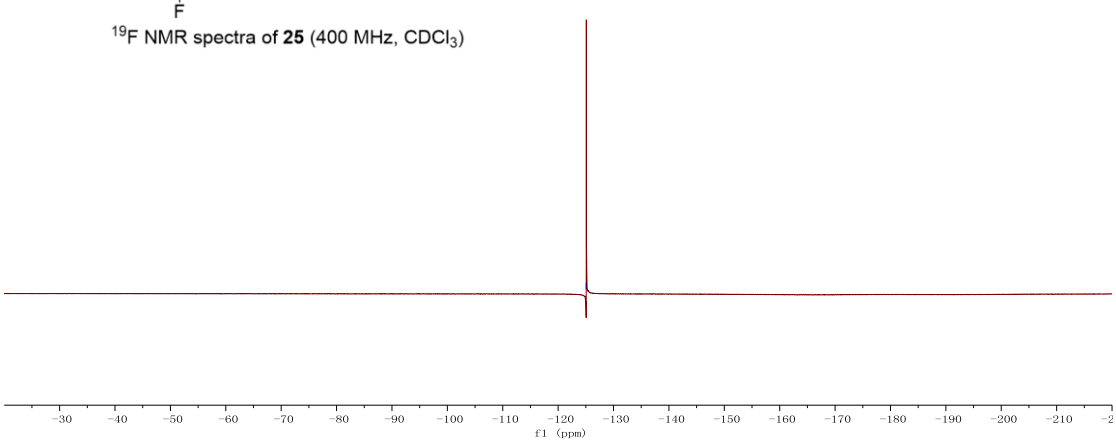
^{1}H NMR spectra of **25** (400 MHz, $CDCl_3$)



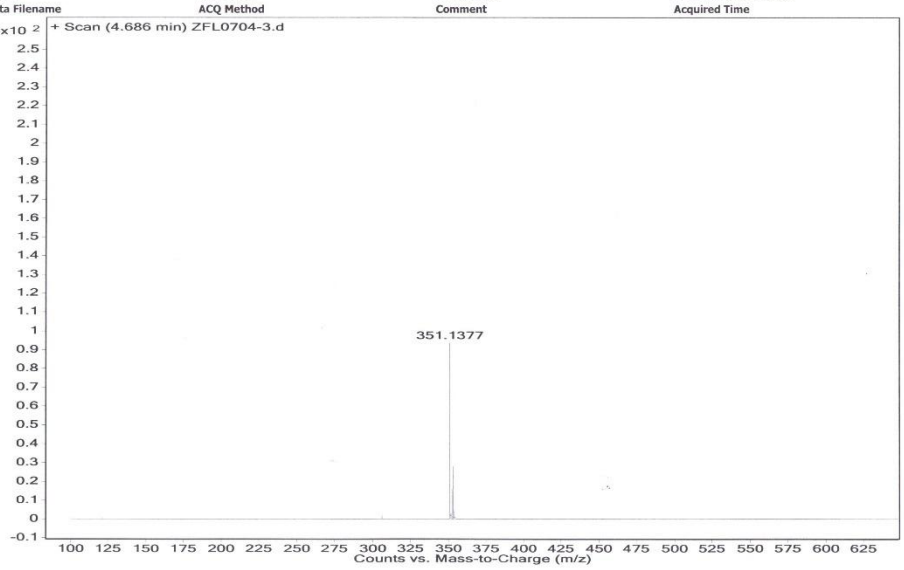
^{13}C {HNMR} spectra of **25** (101 MHz, $CDCl_3$)

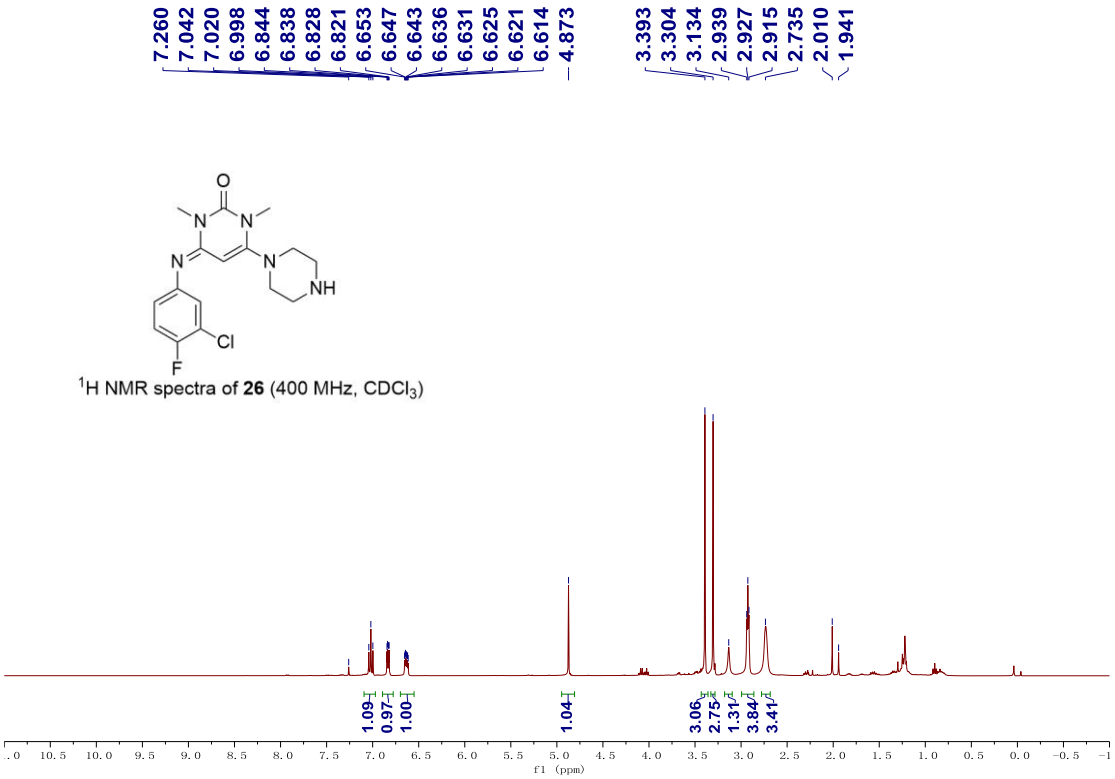


^{19}F NMR spectra of **25** (400 MHz, $CDCl_3$)

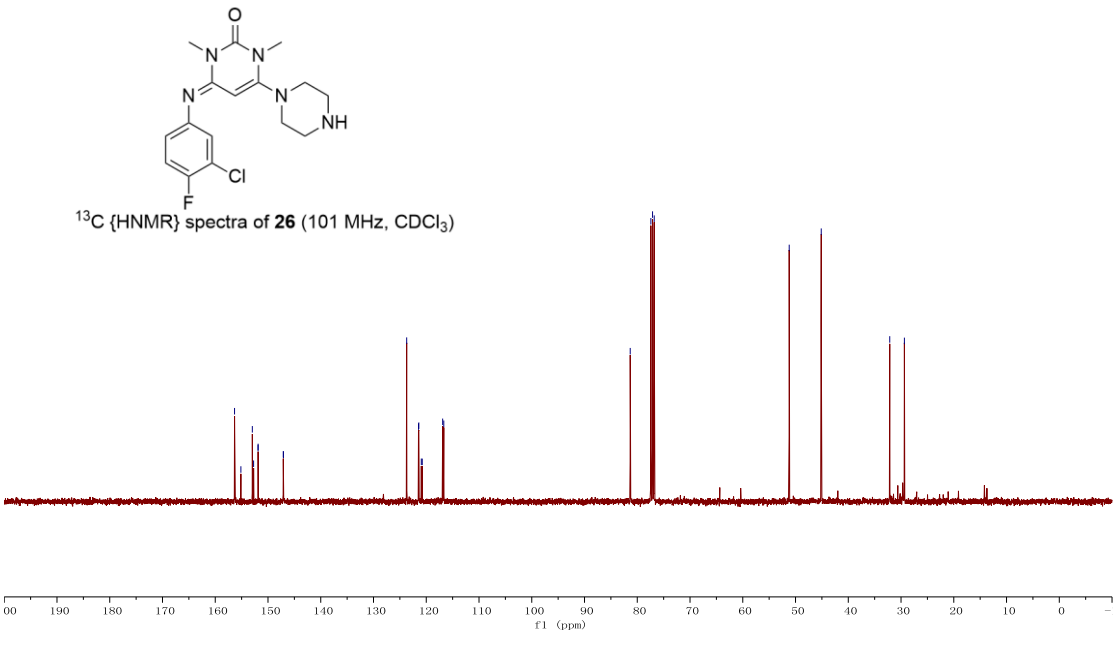


Sample Name	Position	Instrument Name	User Name
Inj Vol	InjPosition	SampleType	IRM Calibration Status
Data Filename	ACQ Method	Comment	Acquired Time





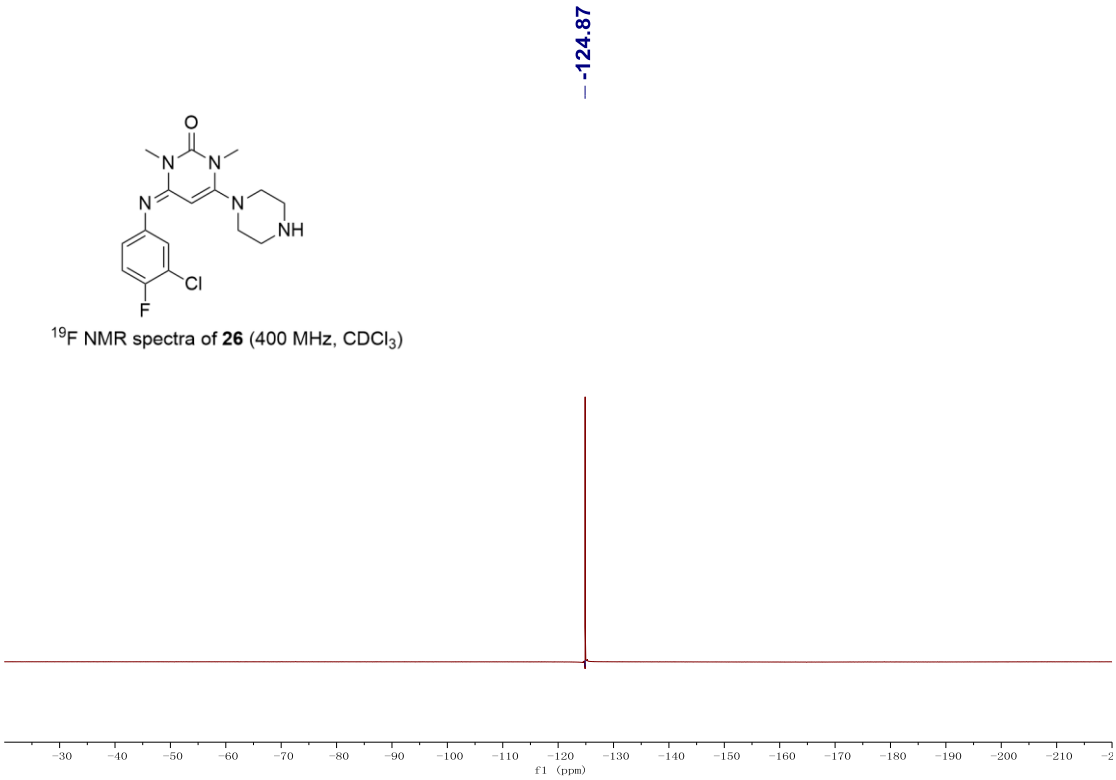
^{1}H NMR spectra of **26** (400 MHz, $CDCl_3$)

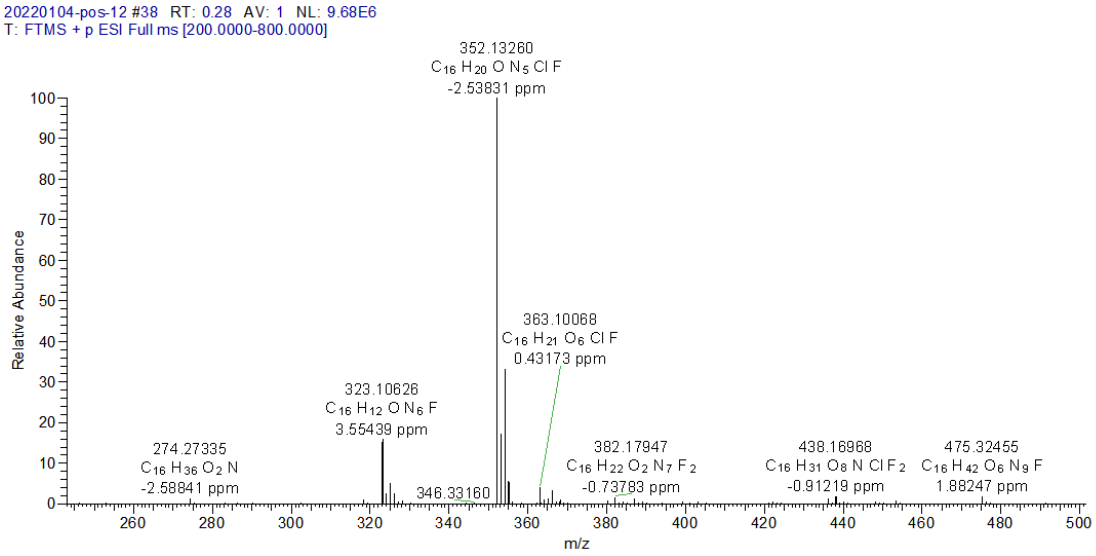


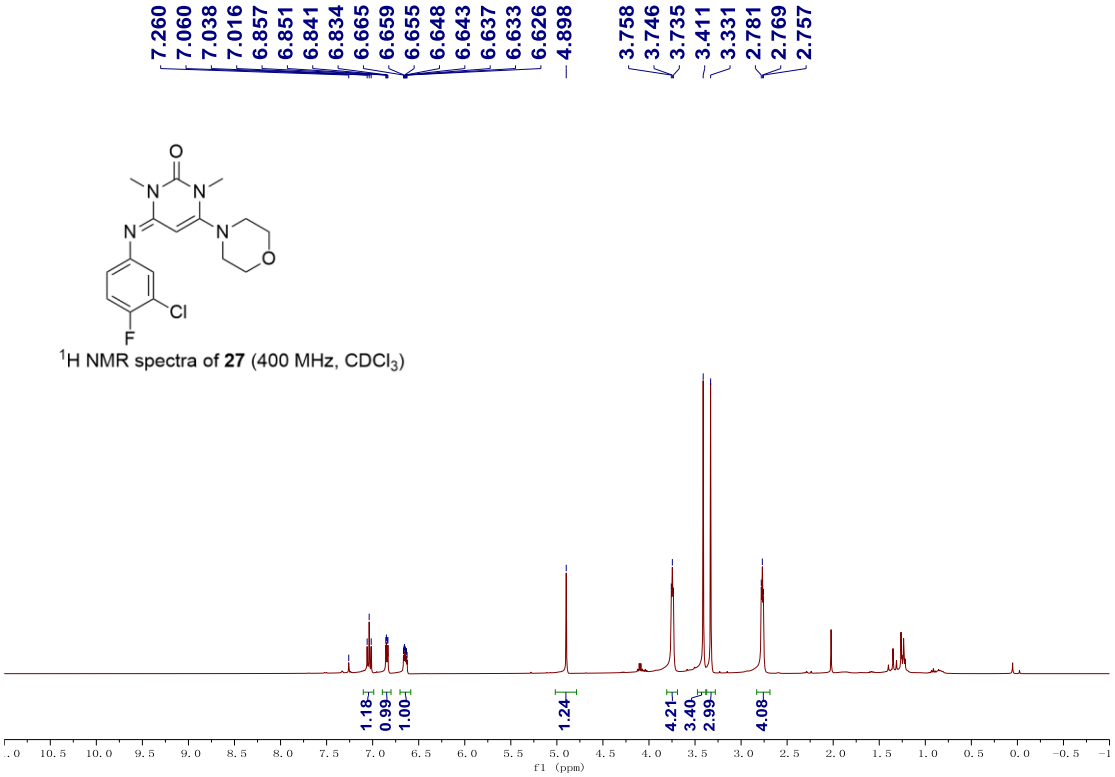
^{13}C {HNMR} spectra of **26** (101 MHz, $CDCl_3$)

C

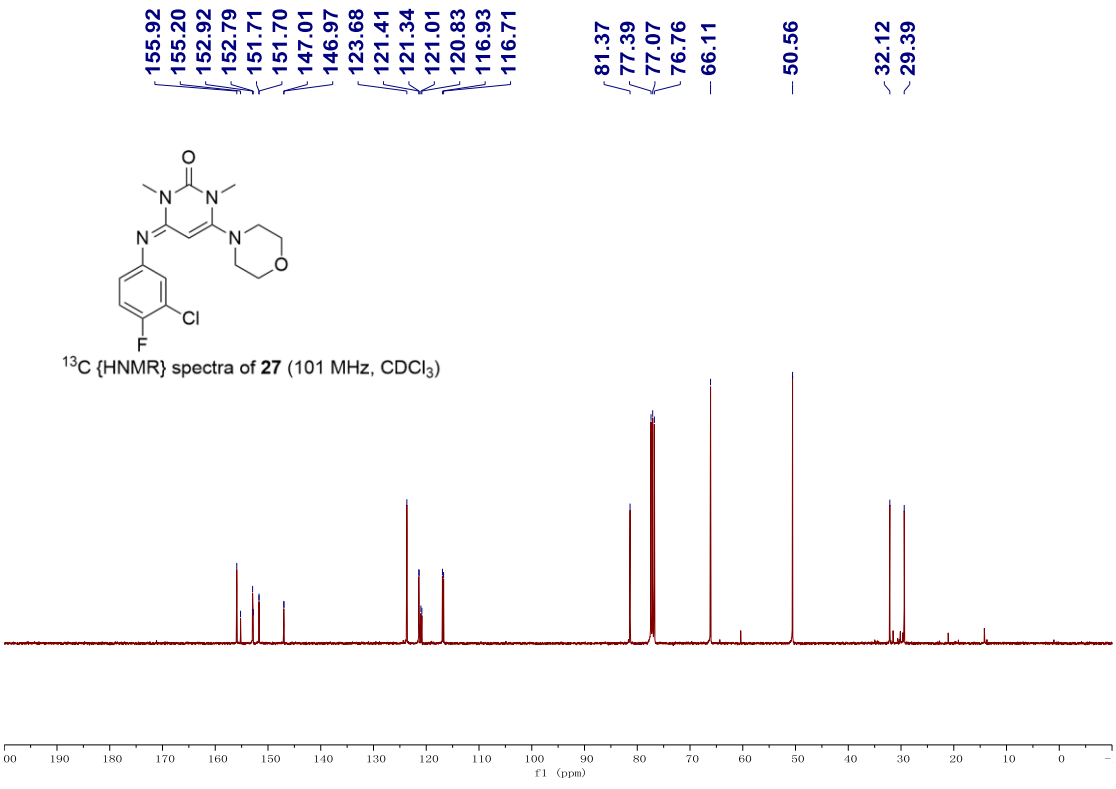
^{19}F NMR spectra of **26** (400 MHz, $CDCl_3$)





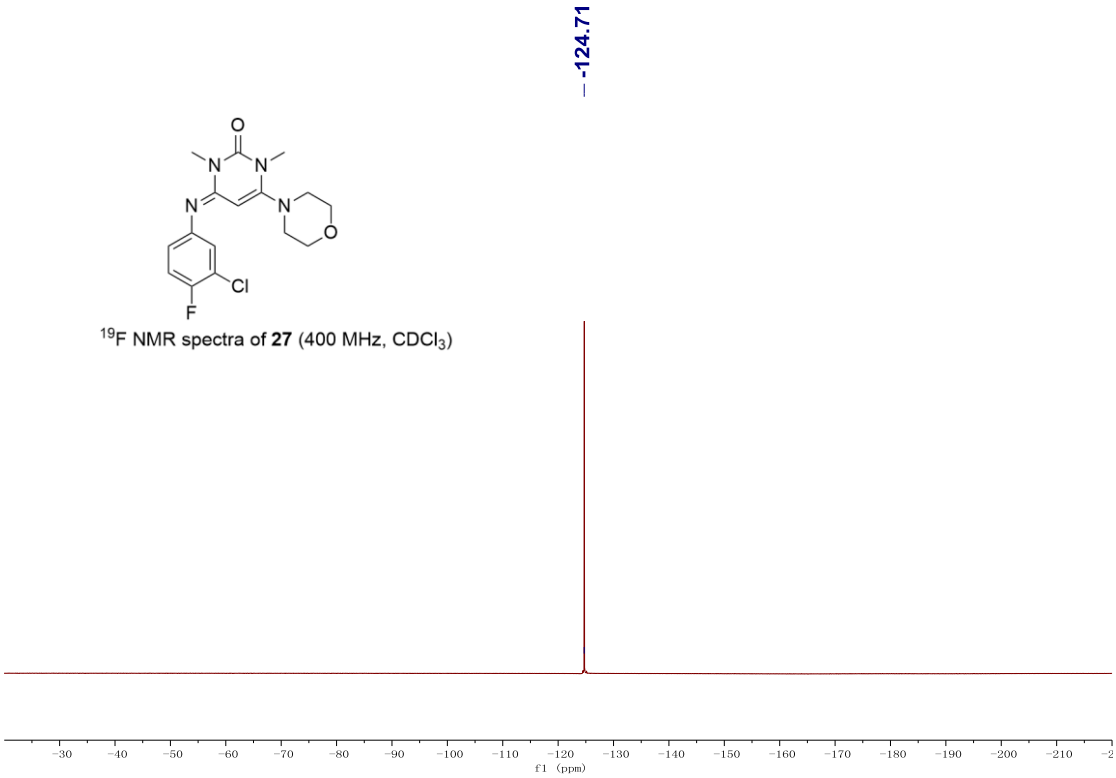


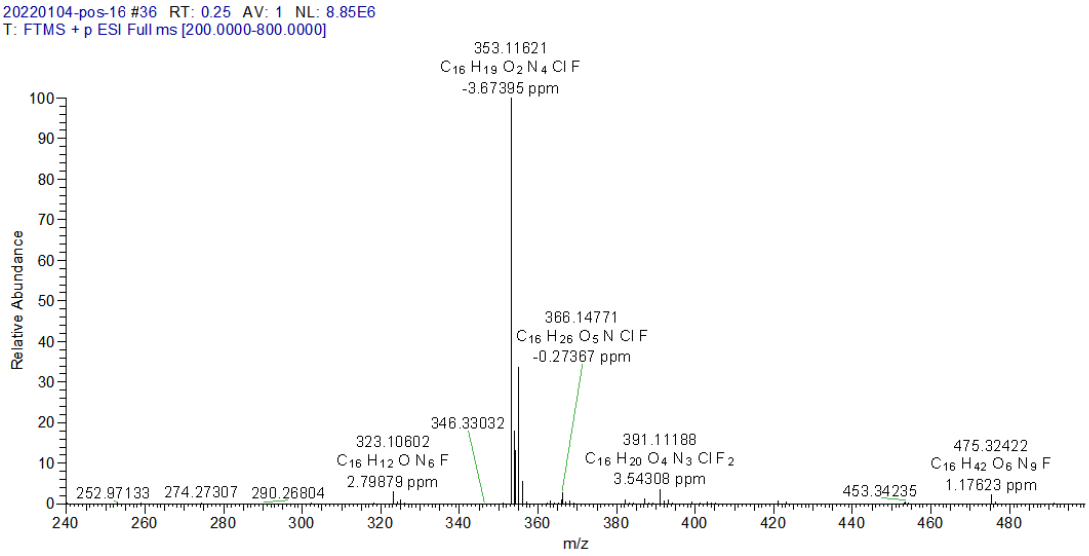
^{1}H NMR spectra of **27** (400 MHz, $CDCl_3$)

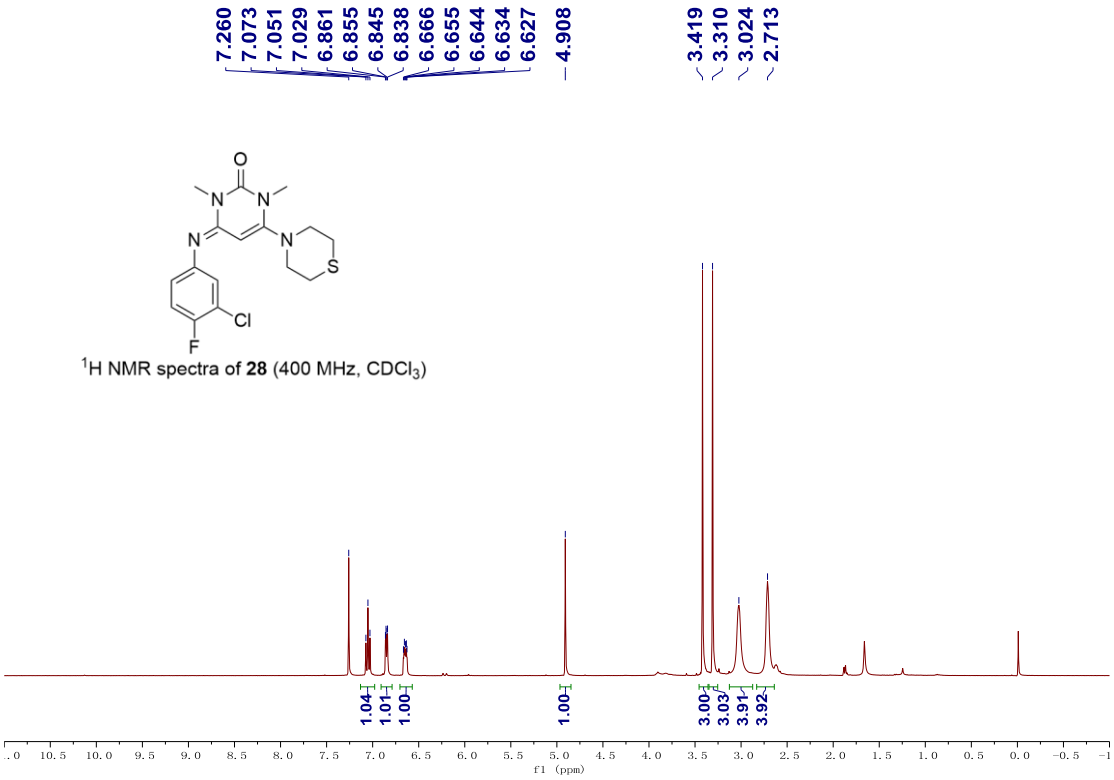


^{13}C {HNMR} spectra of **27** (101 MHz, $CDCl_3$)

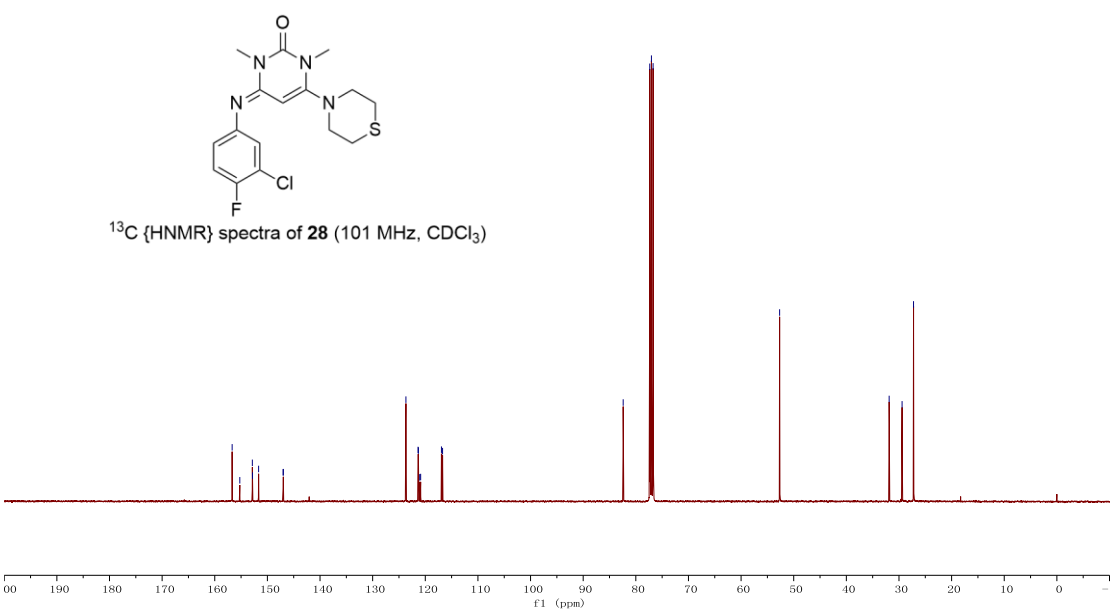
^{19}F NMR spectra of **27** (400 MHz, $CDCl_3$)



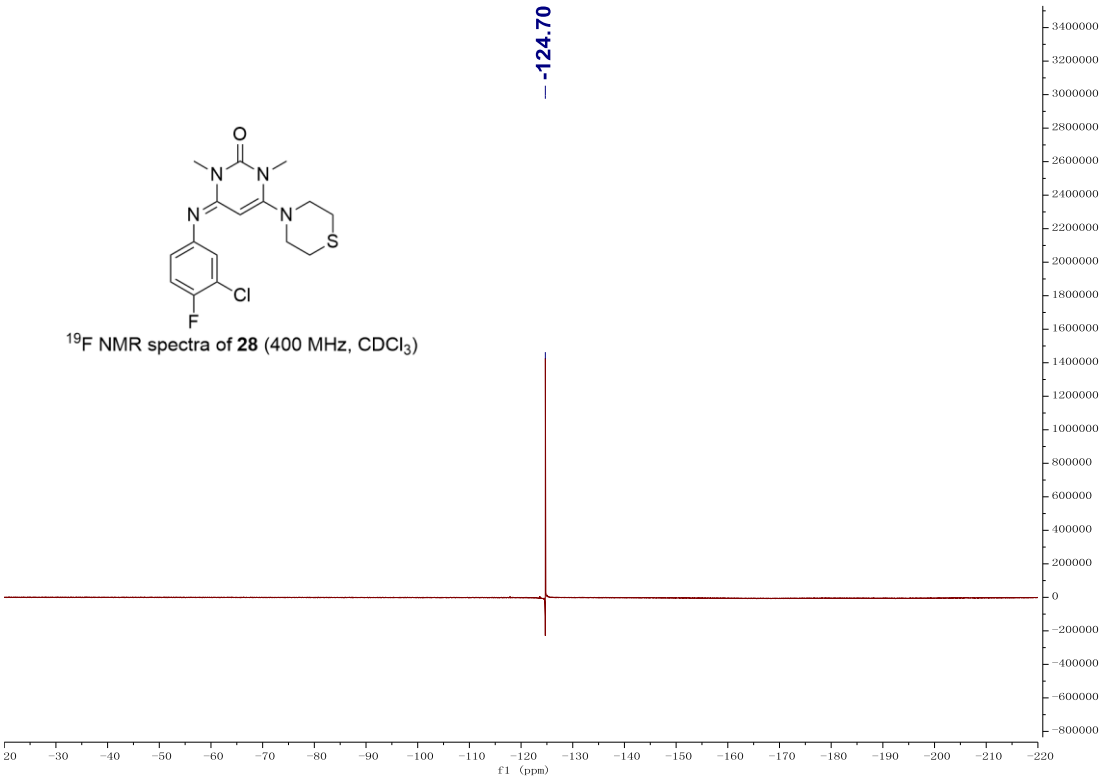




^{1}H NMR spectra of **28** (400 MHz, $CDCl_3$)



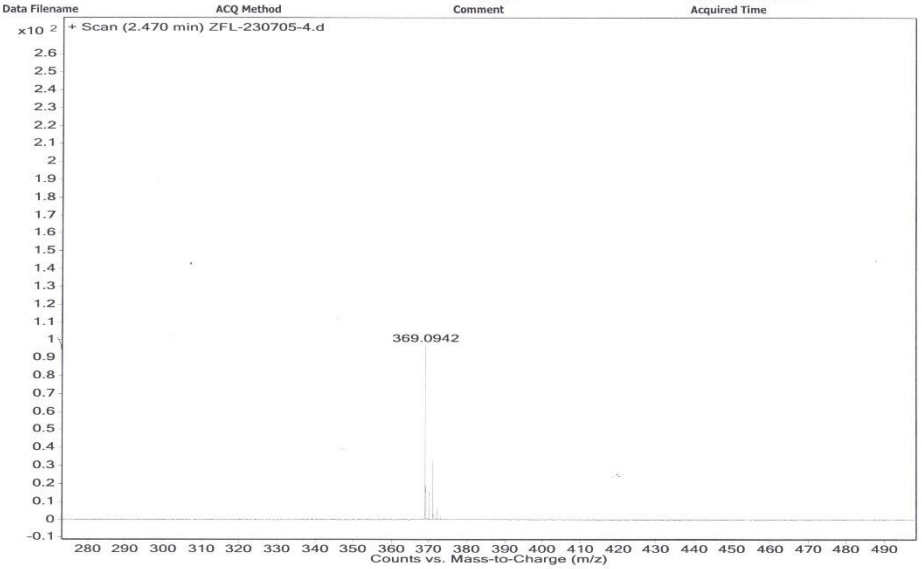
^{13}C {HNMR} spectra of **28** (101 MHz, $CDCl_3$)

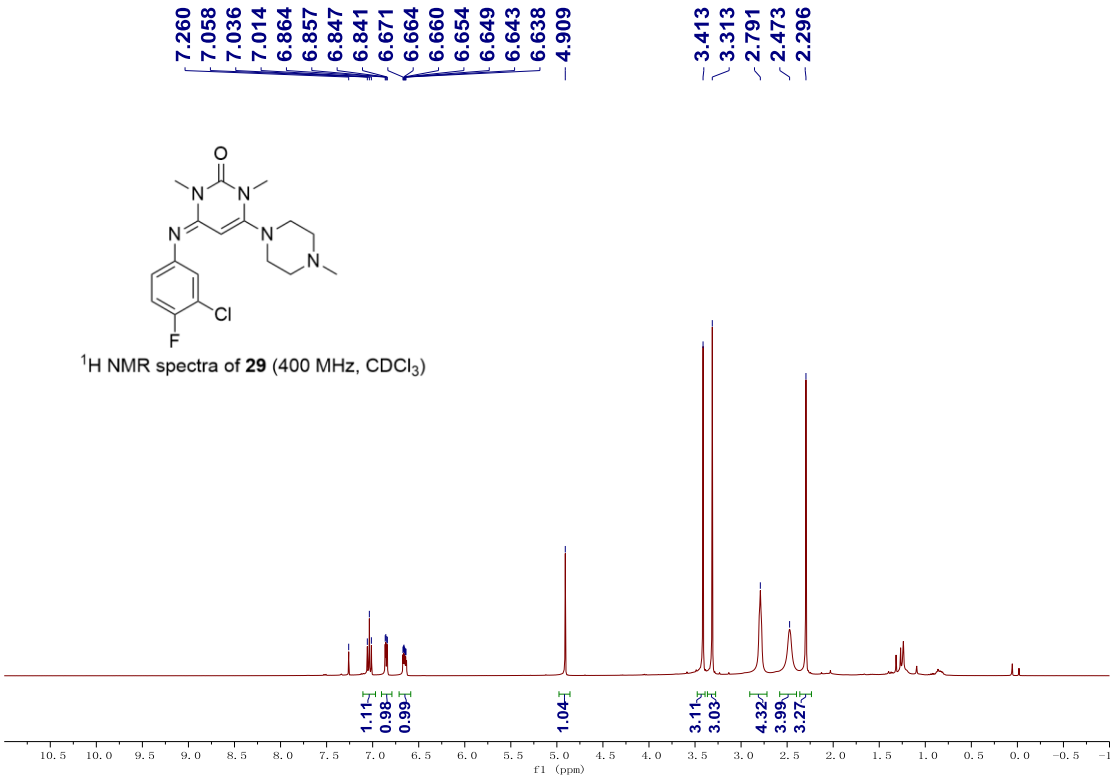


^{19}F NMR spectra of **28** (400 MHz, $CDCl_3$)

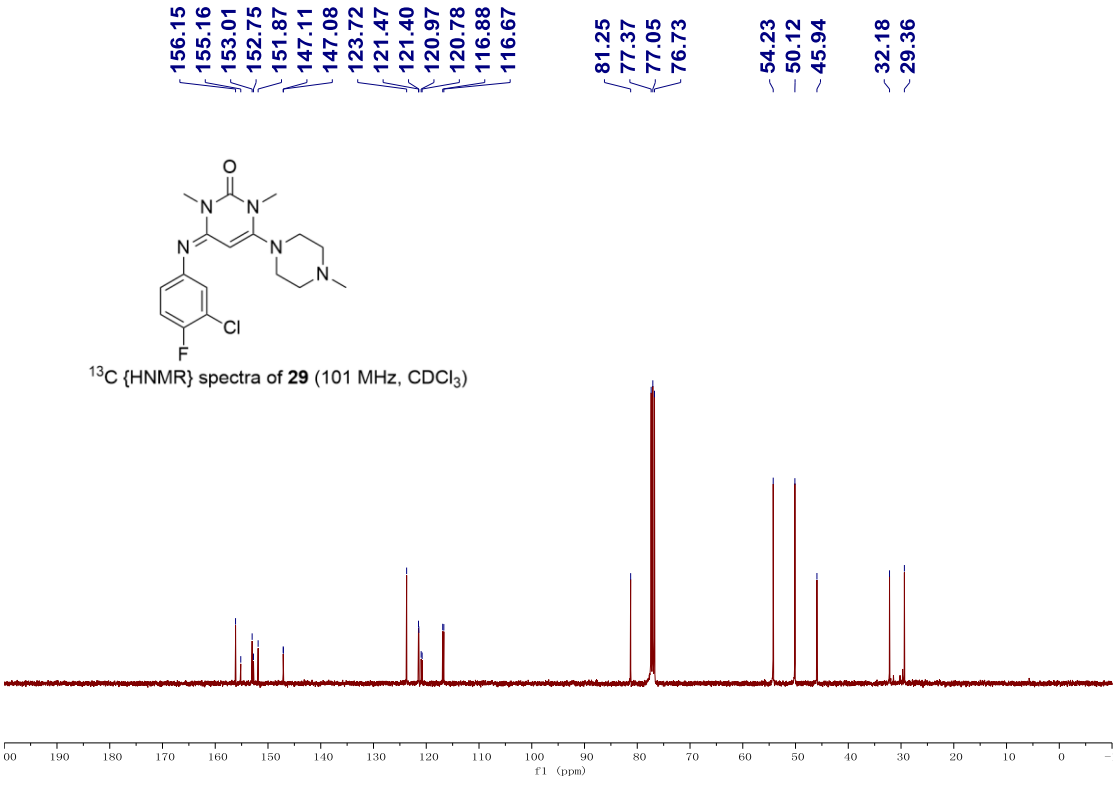
19

Sample Name	Position	Instrument Name	User Name
Inj Vol	InjPosition	SampleType	IRM Calibration Status
Data Filename	ACQ Method	Comment	Acquired Time

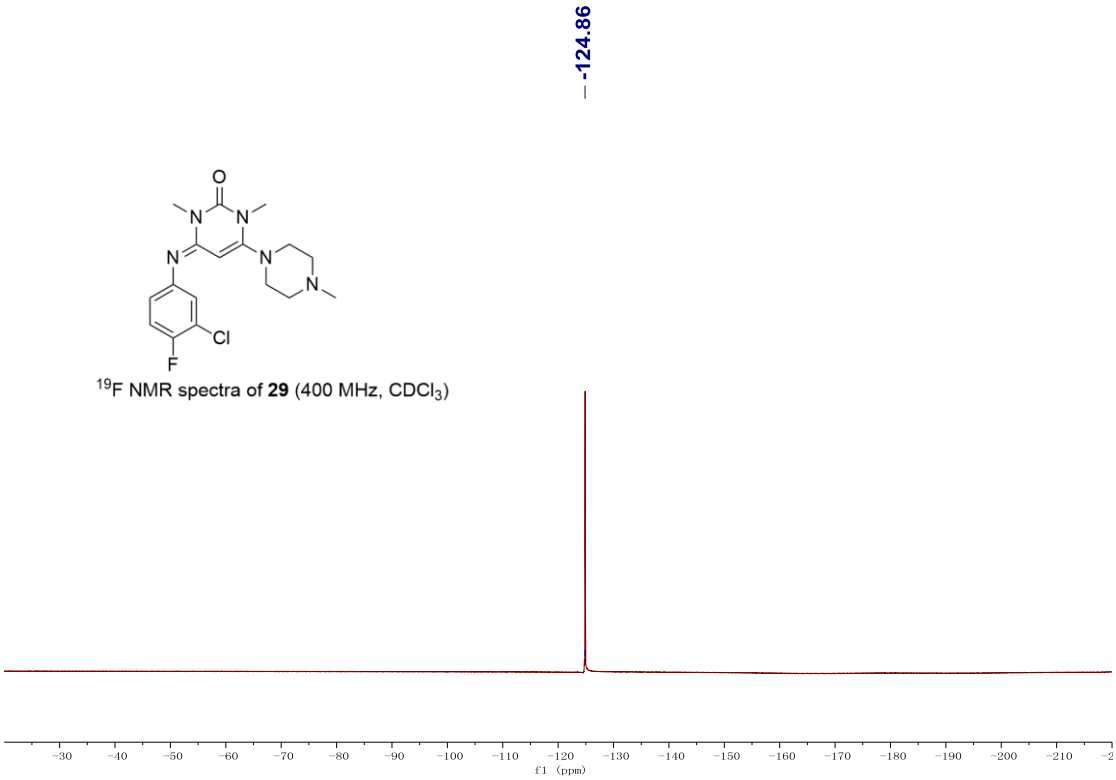




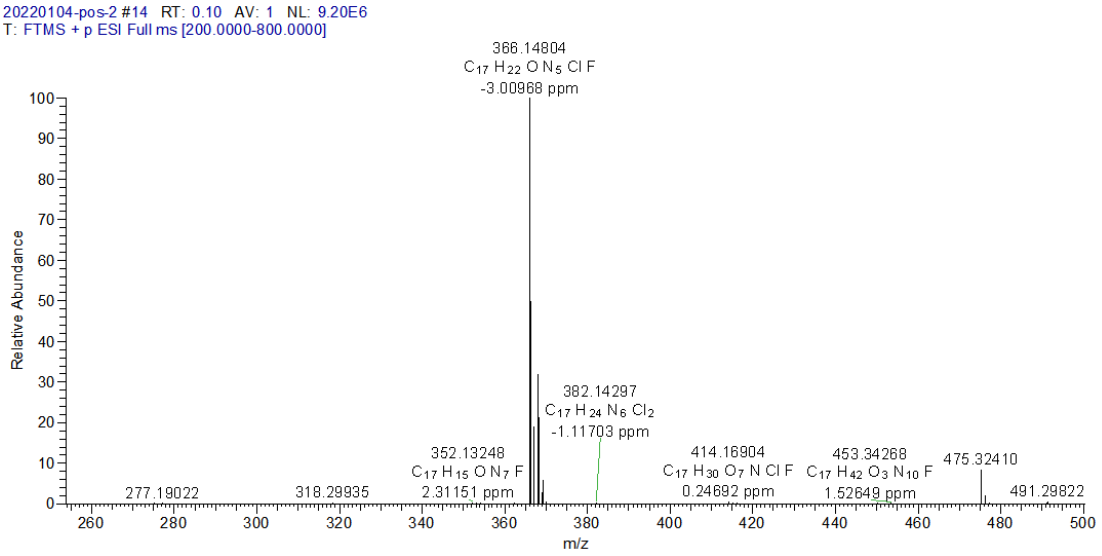
^{1}H NMR spectra of **29** (400 MHz, $CDCl_3$)

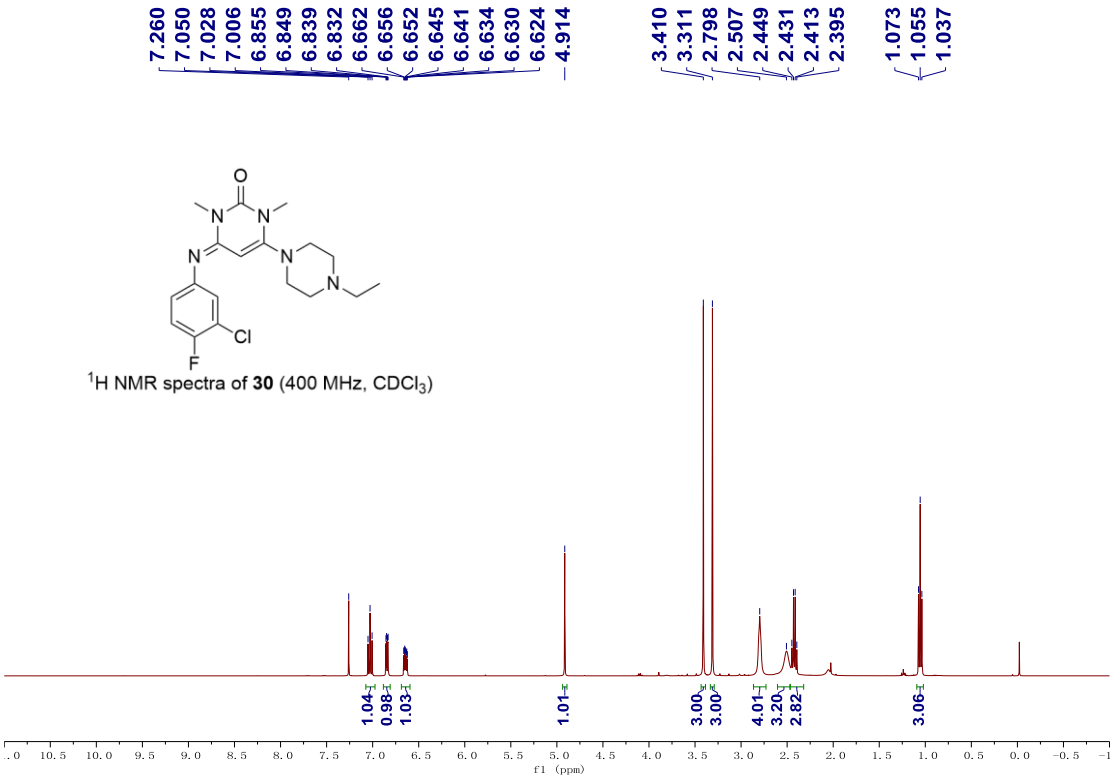


^{13}C {HNMR} spectra of **29** (101 MHz, $CDCl_3$)

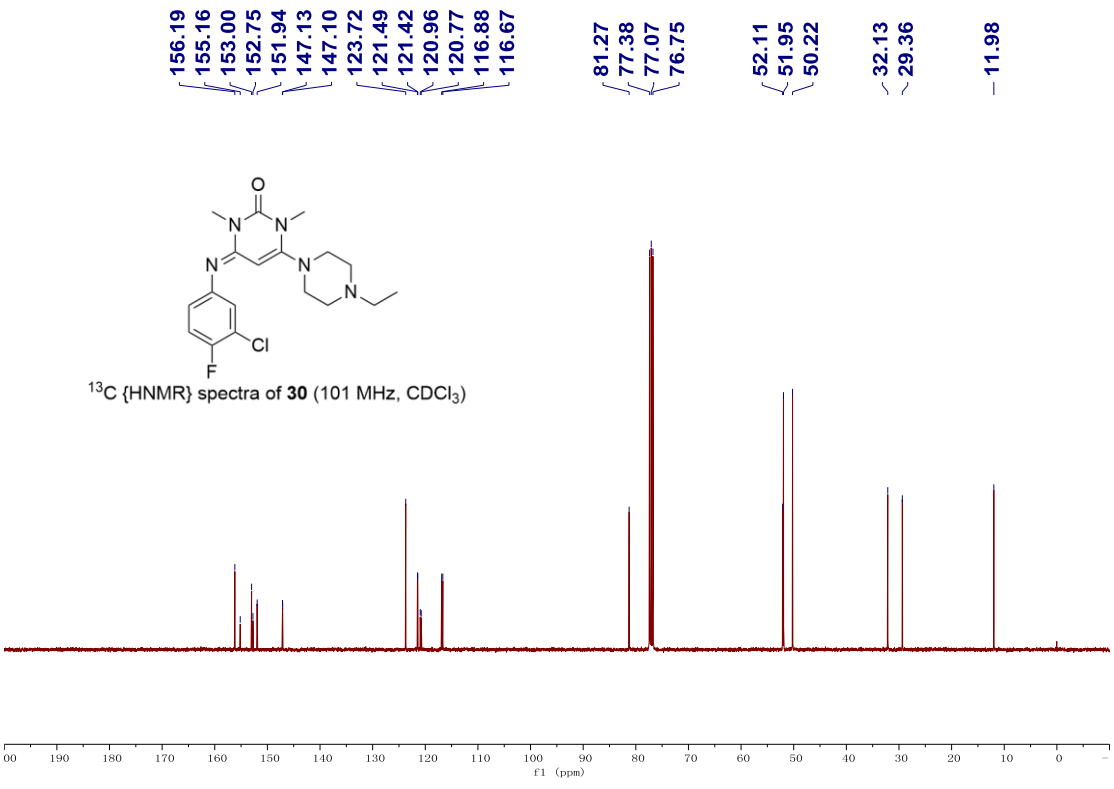


^{19}F NMR spectra of **29** (400 MHz, $CDCl_3$)

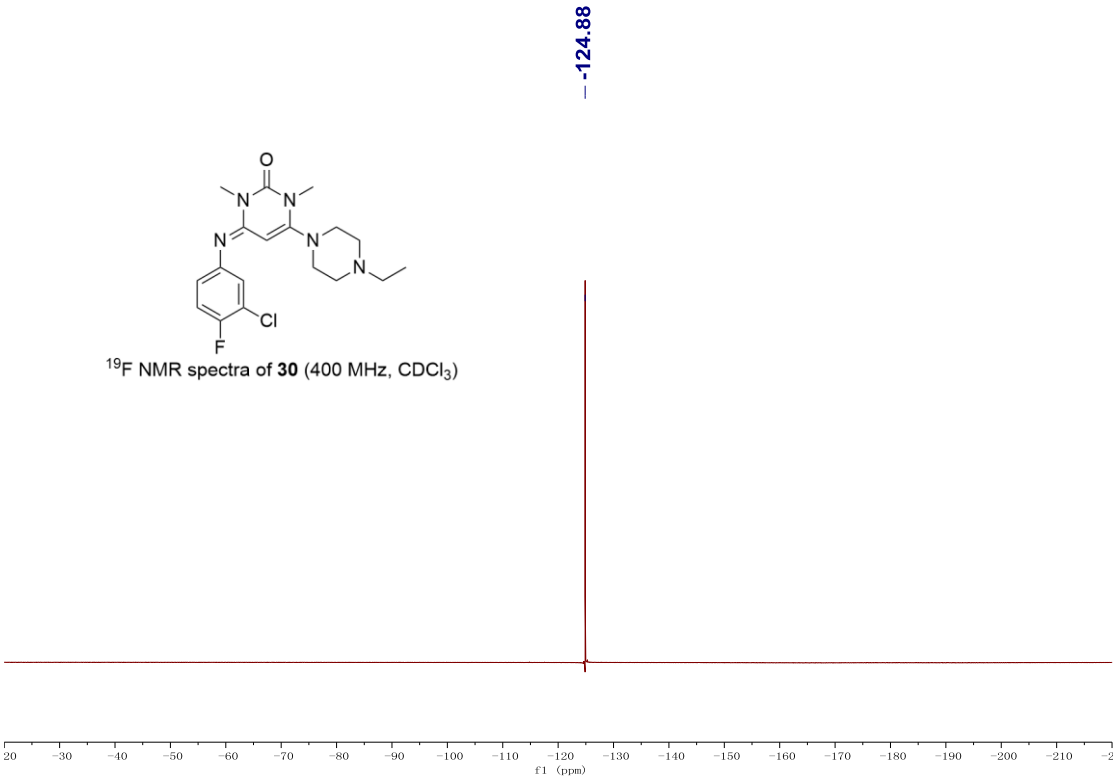




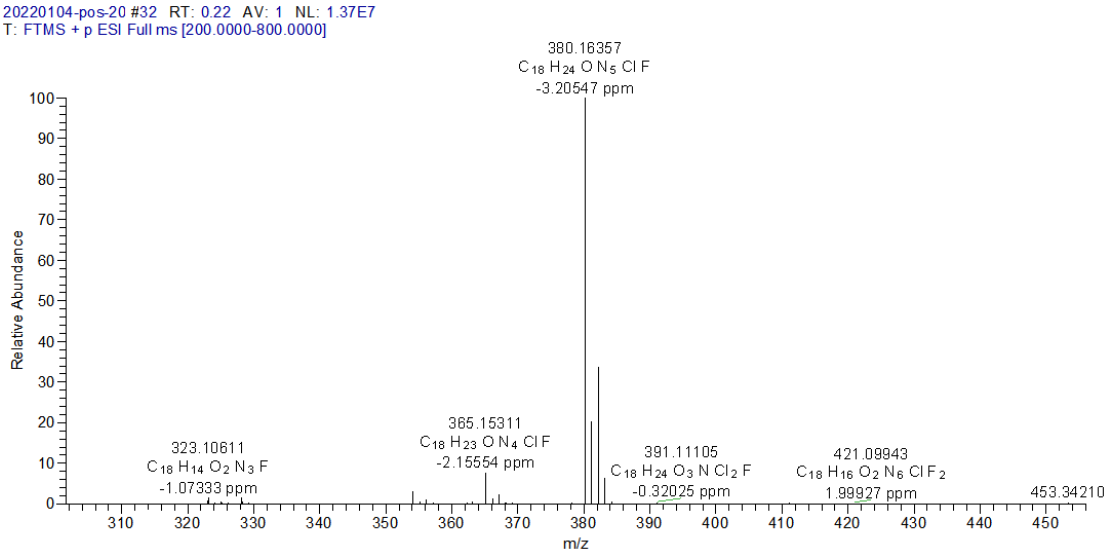
^{1}H NMR spectra of **30** (400 MHz, $CDCl_3$)

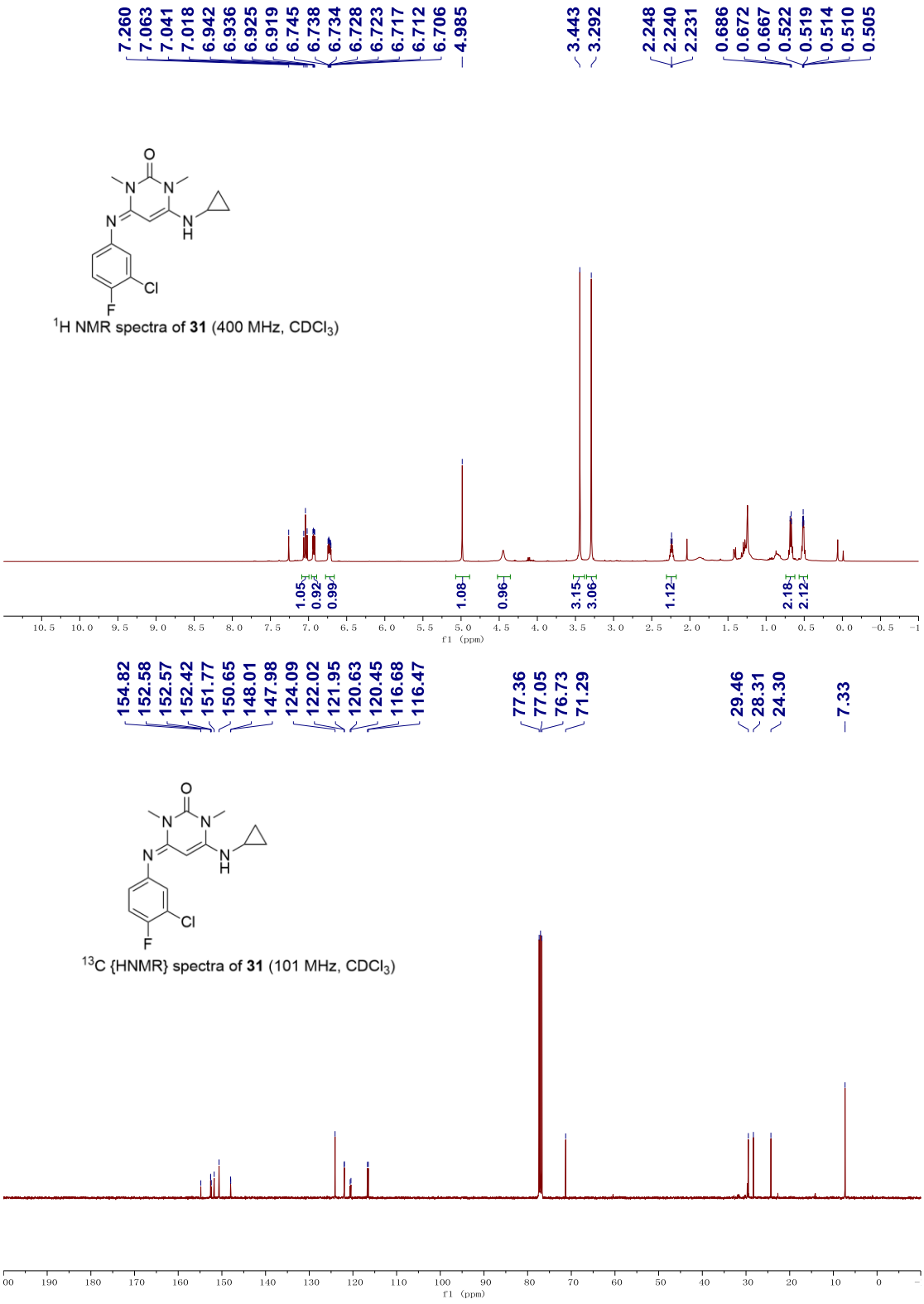


^{13}C {HNMR} spectra of **30** (101 MHz, $CDCl_3$)



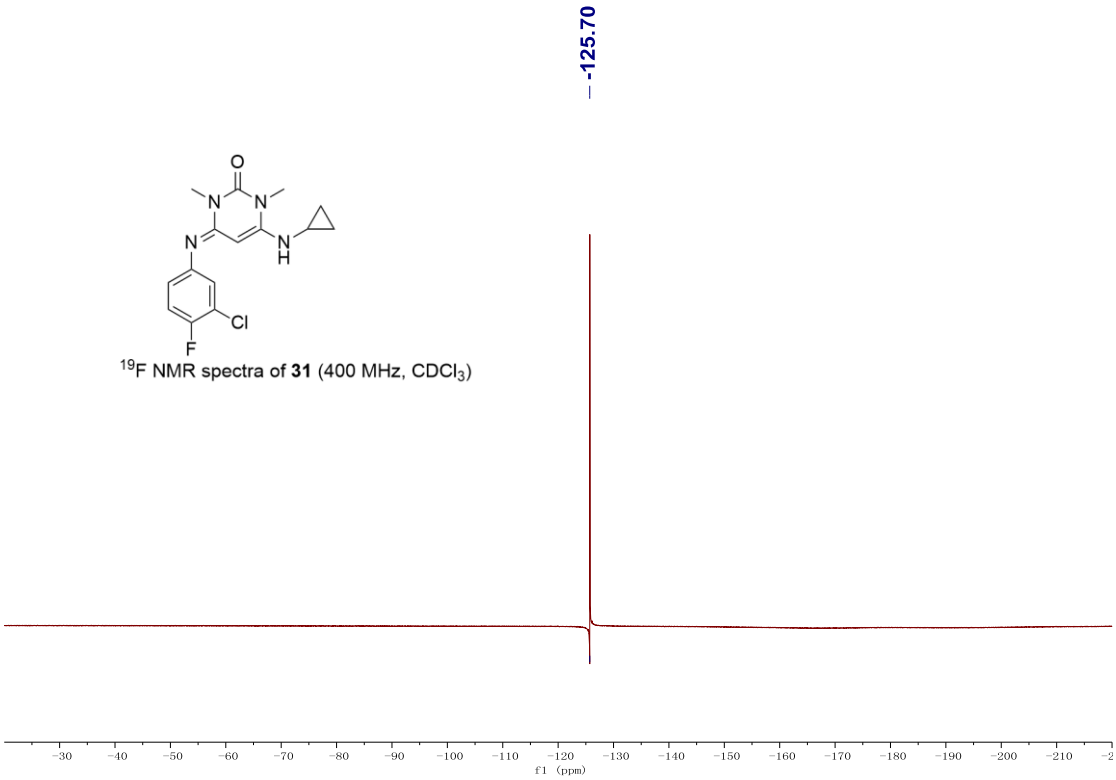
^{19}F NMR spectra of **30** (400 MHz, $CDCl_3$)



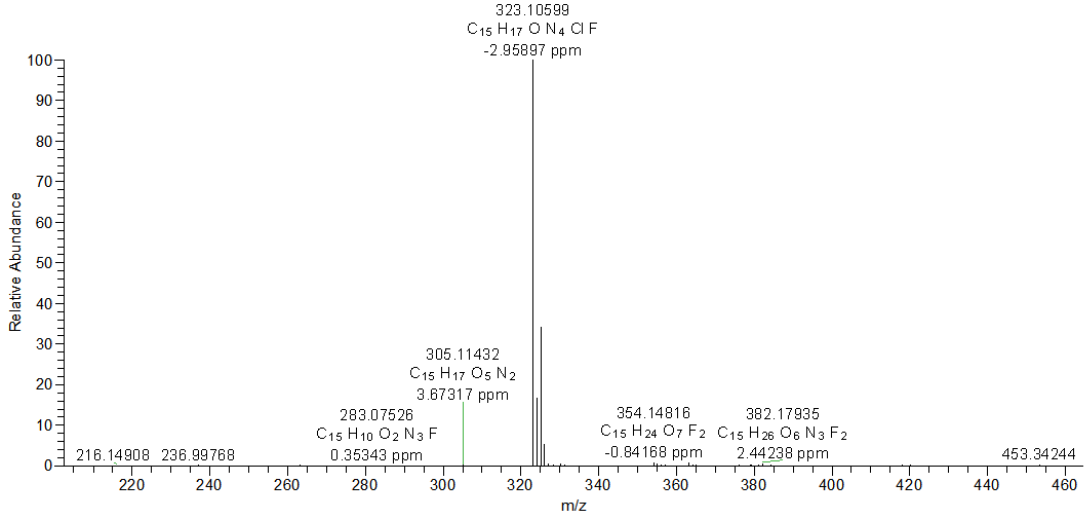


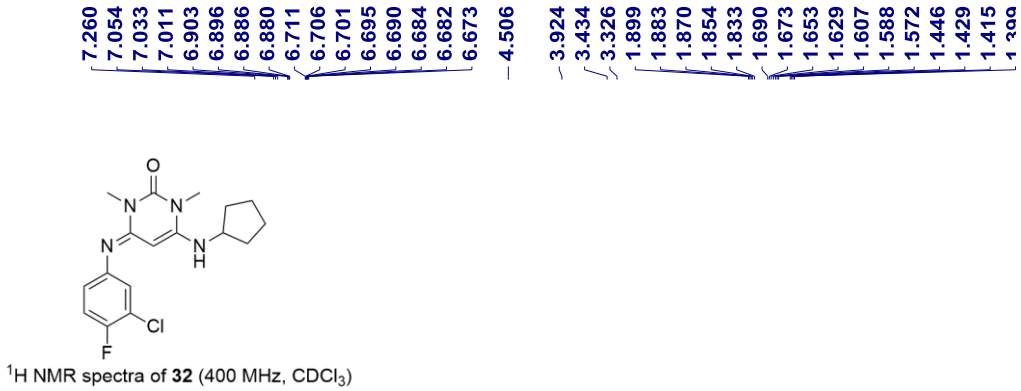
^{1}H NMR spectra of **31** (400 MHz, $CDCl_3$)

^{13}C {HNMR} spectra of **31** (101 MHz, $CDCl_3$)

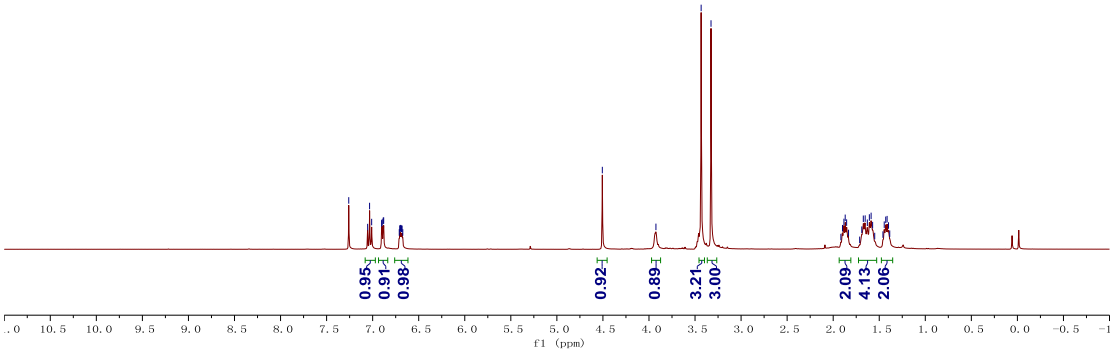


^{19}F NMR spectra of **31** (400 MHz, $CDCl_3$)

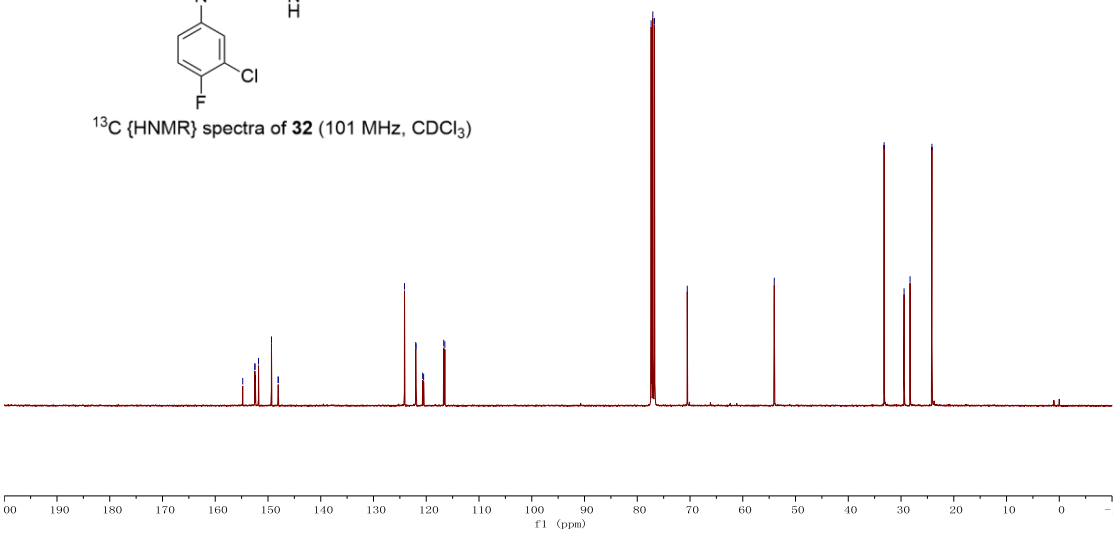


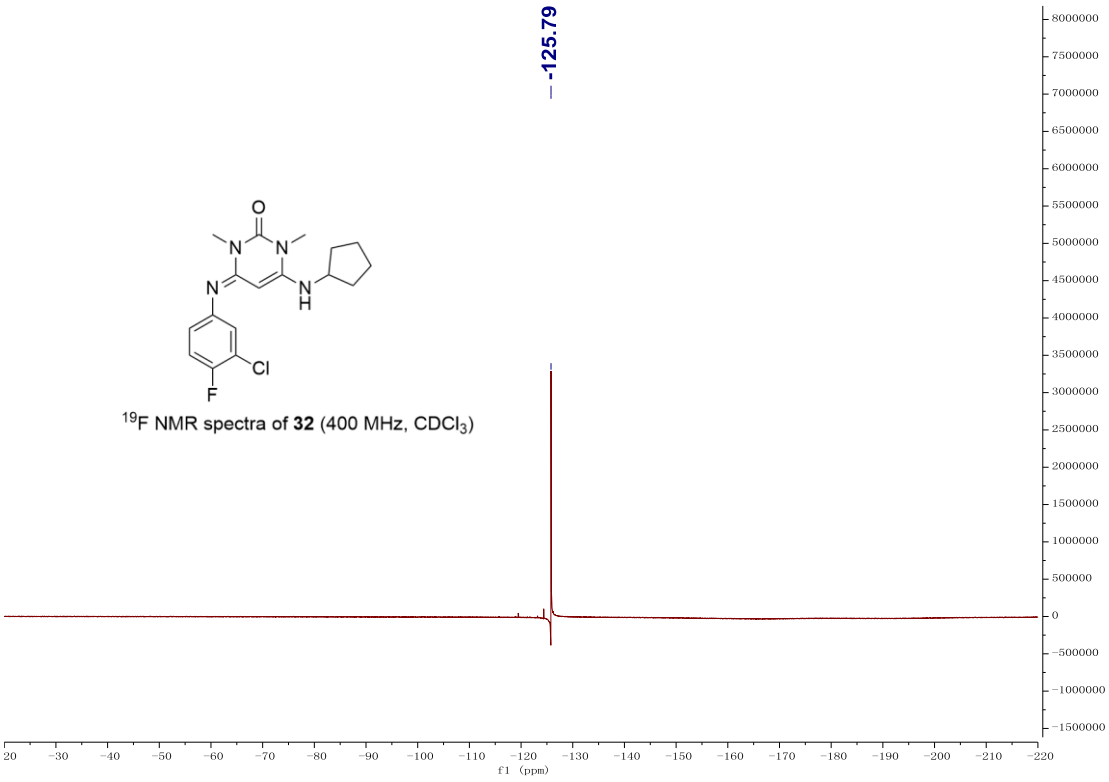


^{1}H NMR spectra of **32** (400 MHz, $CDCl_3$)



^{13}C {HNMR} spectra of **32** (101 MHz, $CDCl_3$)

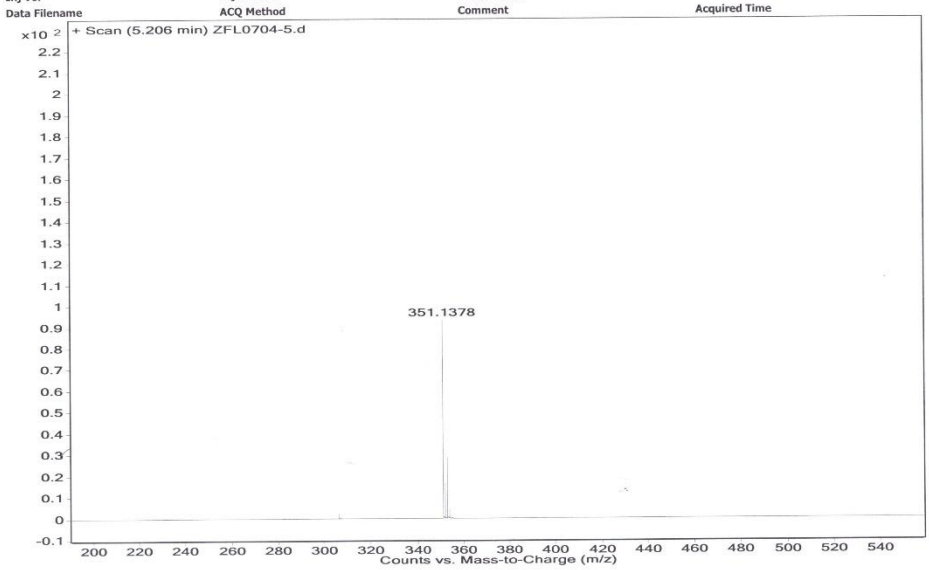


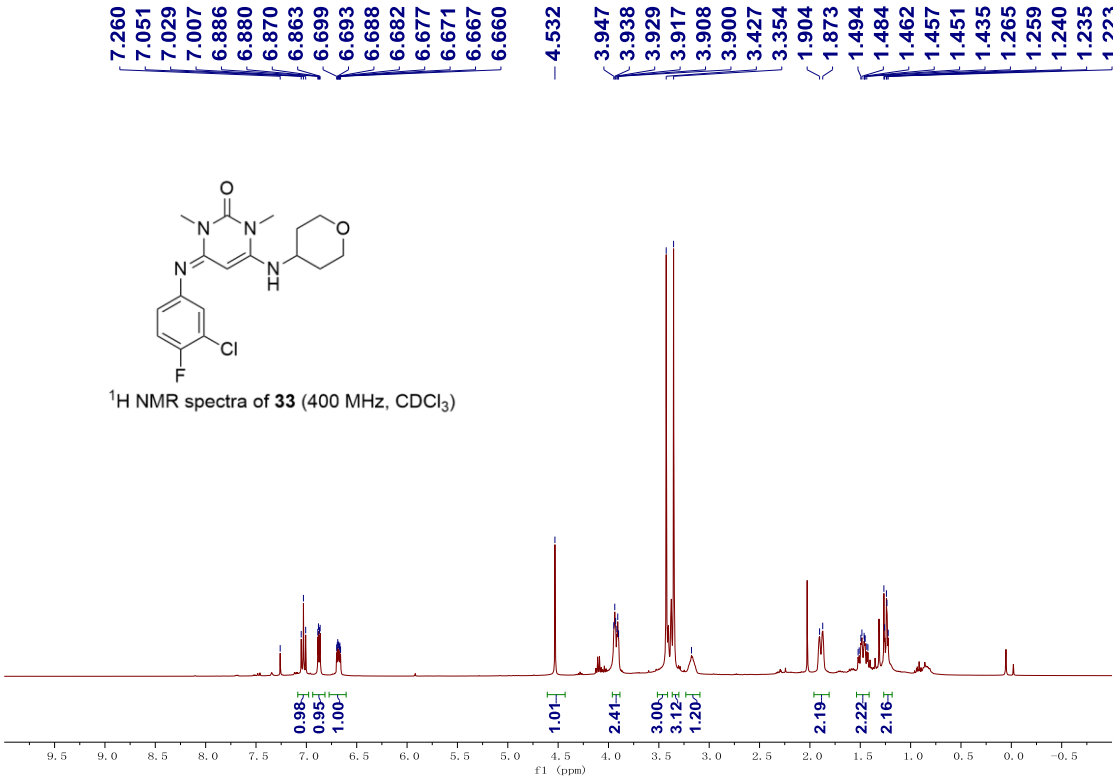


^{19}F NMR spectra of **32** (400 MHz, $CDCl_3$)

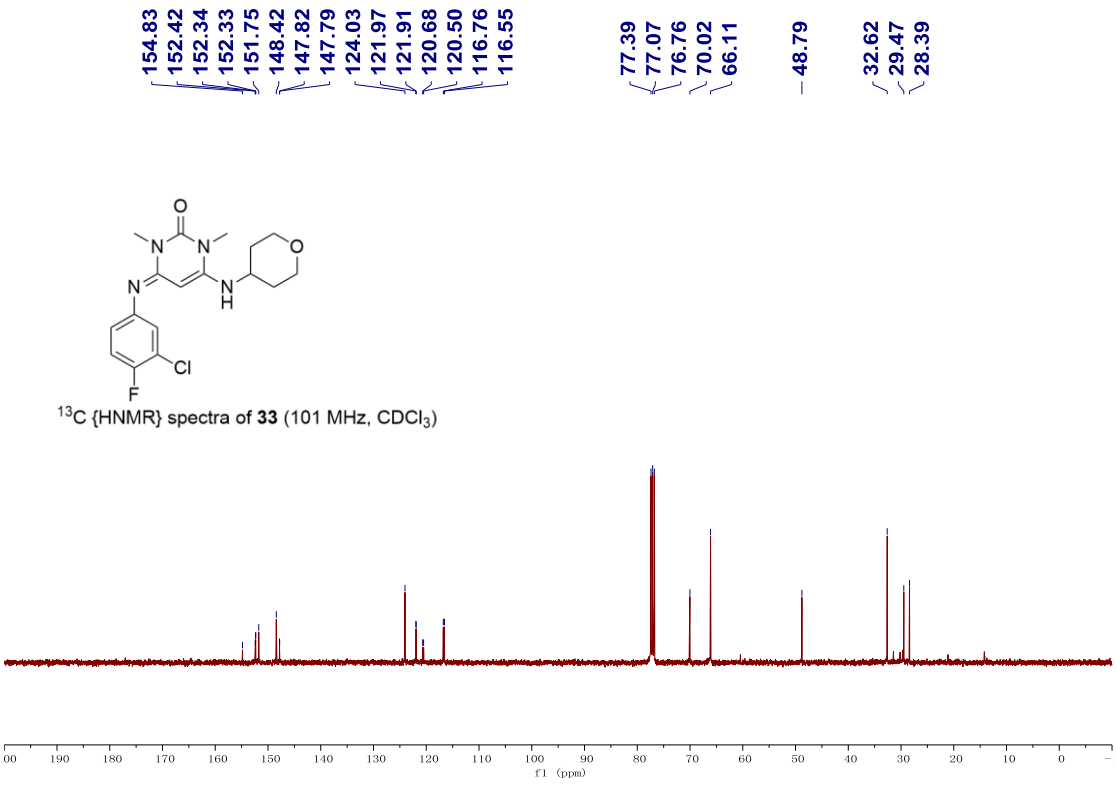
16.

Sample Name	Position	Instrument Name	User Name
Inj Vol	InjPosition	SampleType	IRM Calibration Status
Data Filename	ACQ Method	Comment	Acquired Time



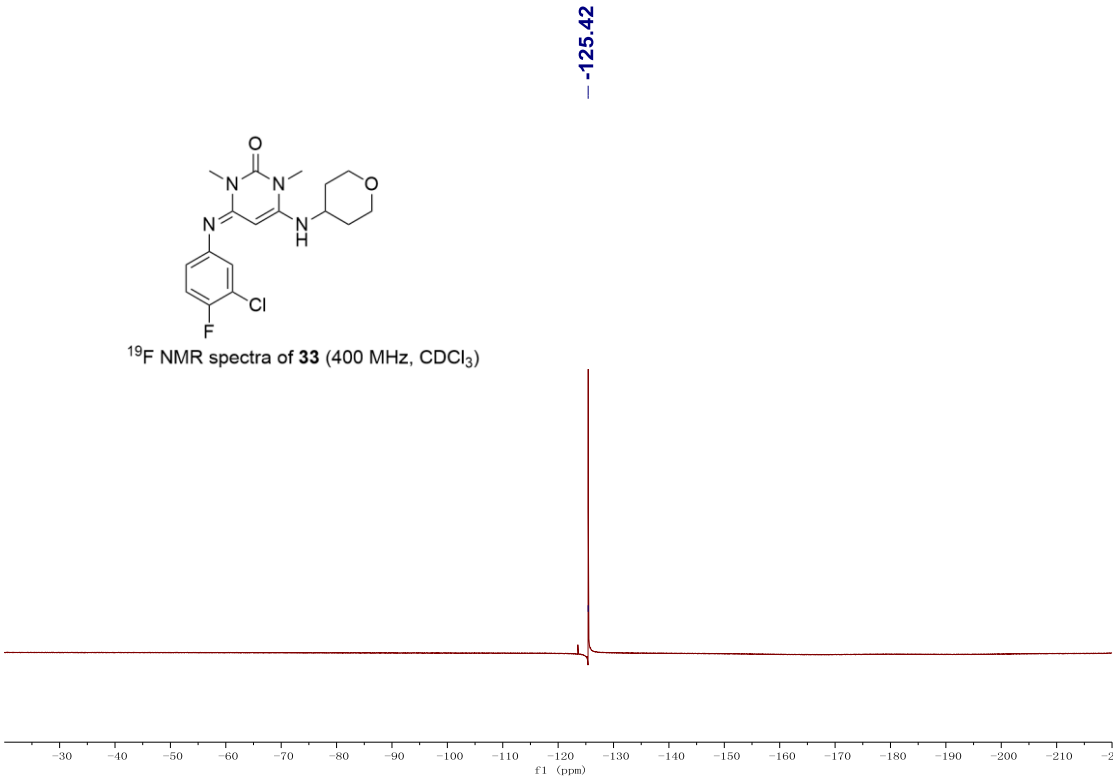


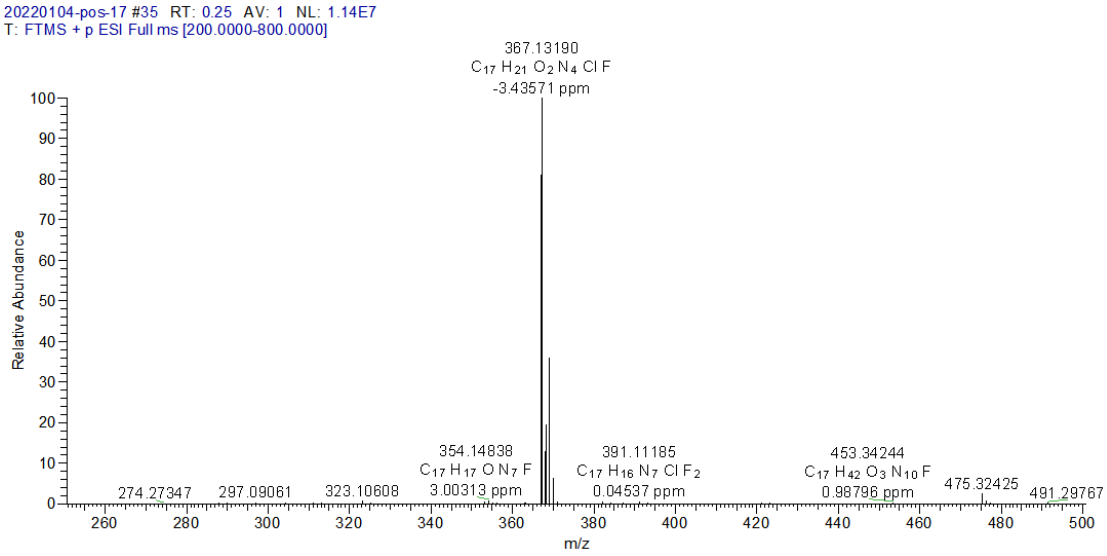
^{1}H NMR spectra of **33** (400 MHz, $CDCl_3$)

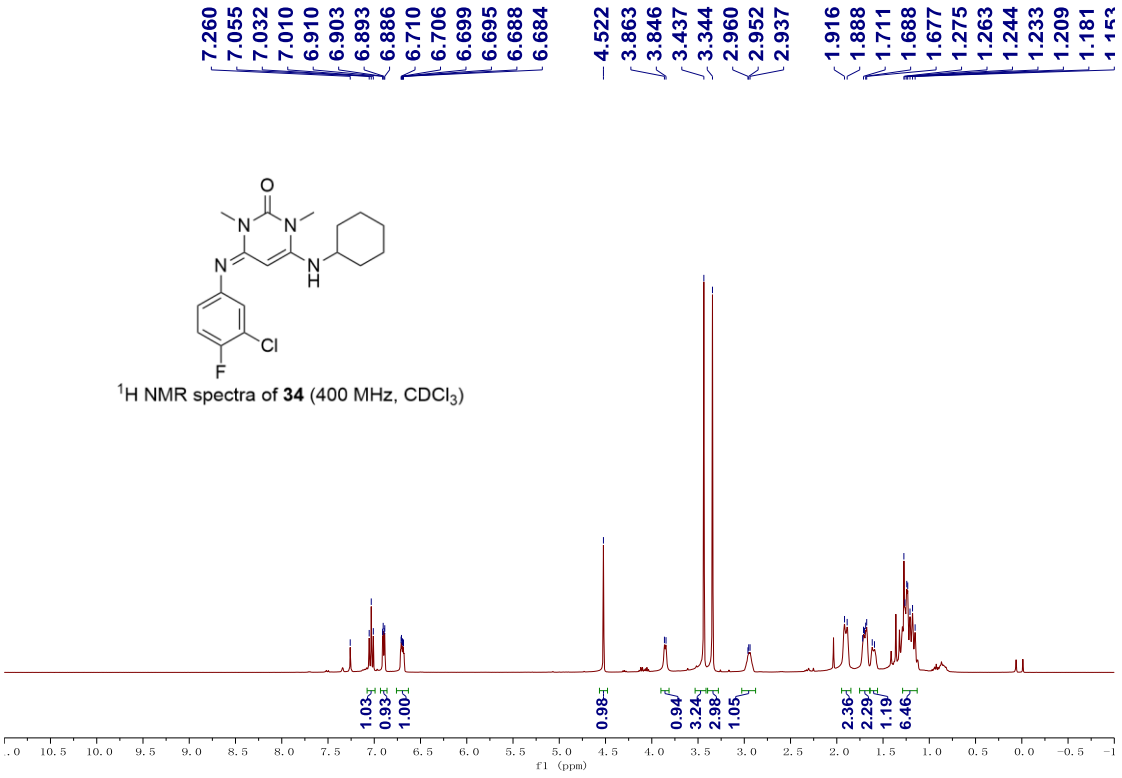


^{13}C {HNMR} spectra of **33** (101 MHz, $CDCl_3$)

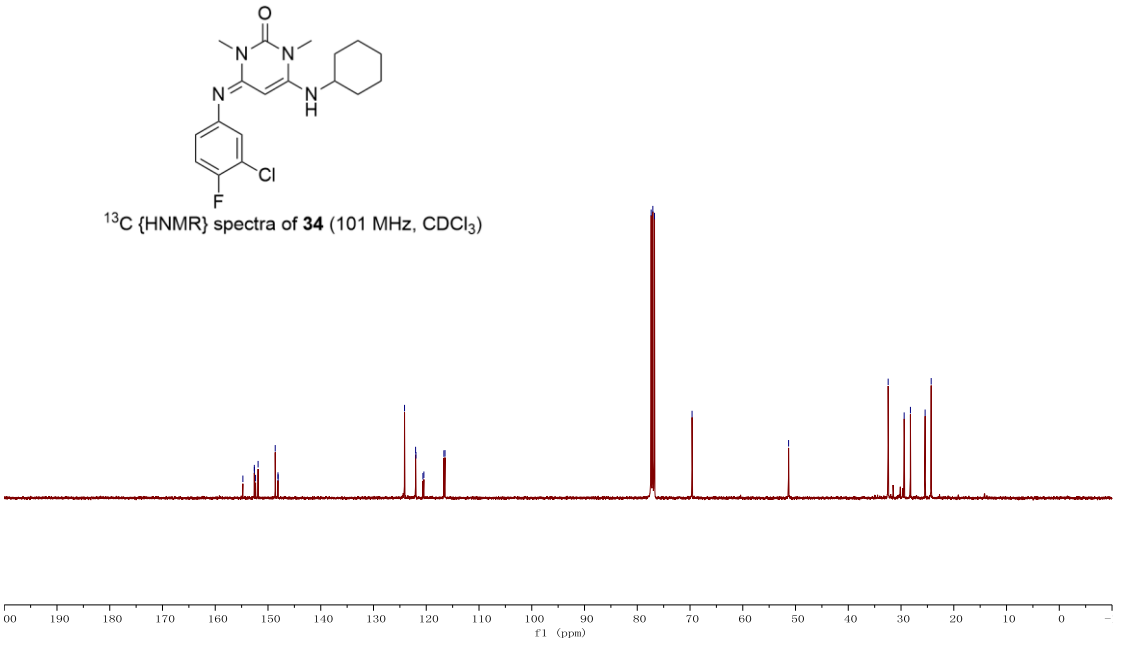
^{19}F NMR spectra of **33** (400 MHz, $CDCl_3$)



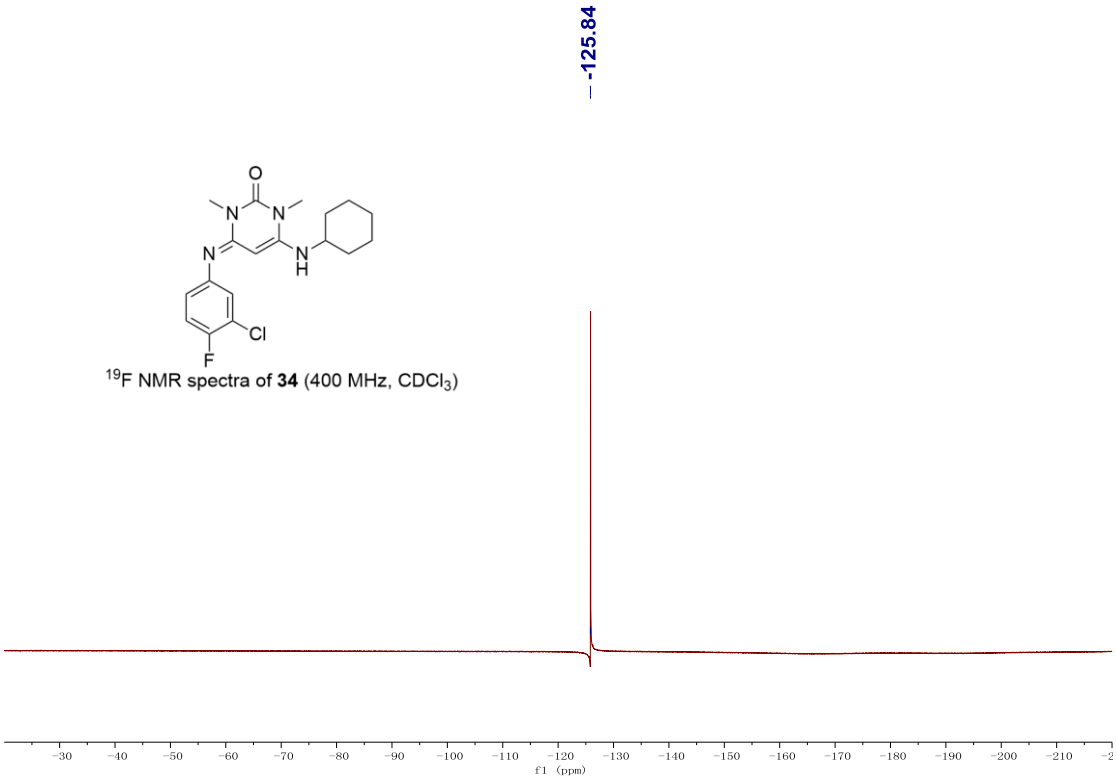




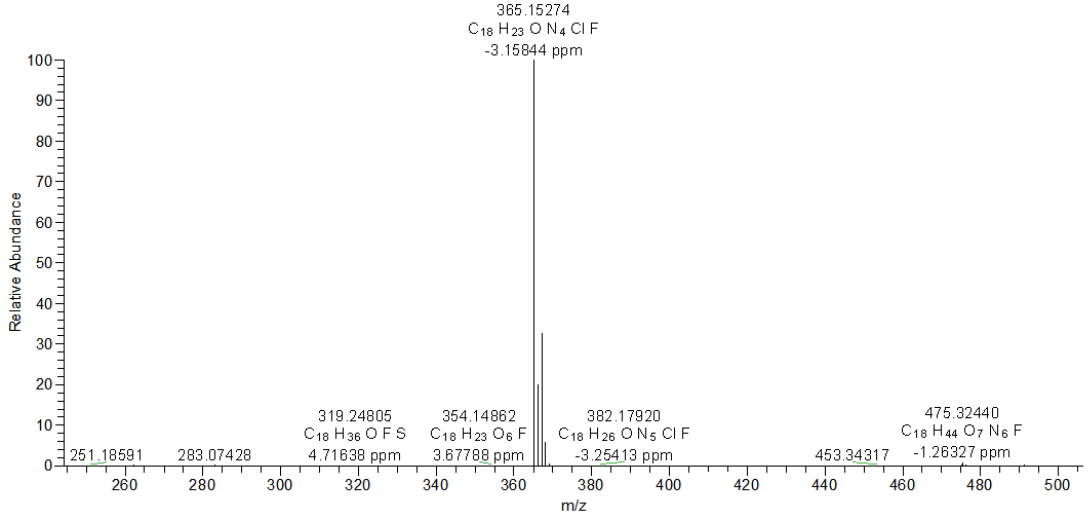
^{1}H NMR spectra of **34** (400 MHz, $CDCl_3$)

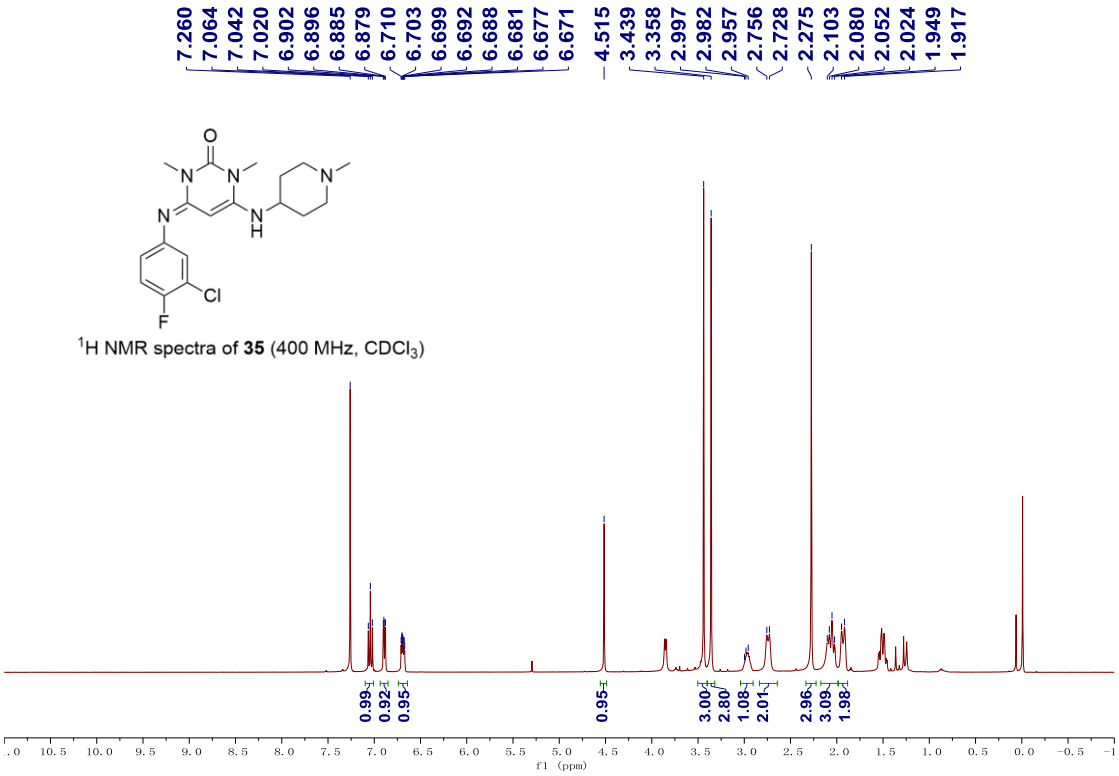


^{13}C {HNMR} spectra of **34** (101 MHz, $CDCl_3$)

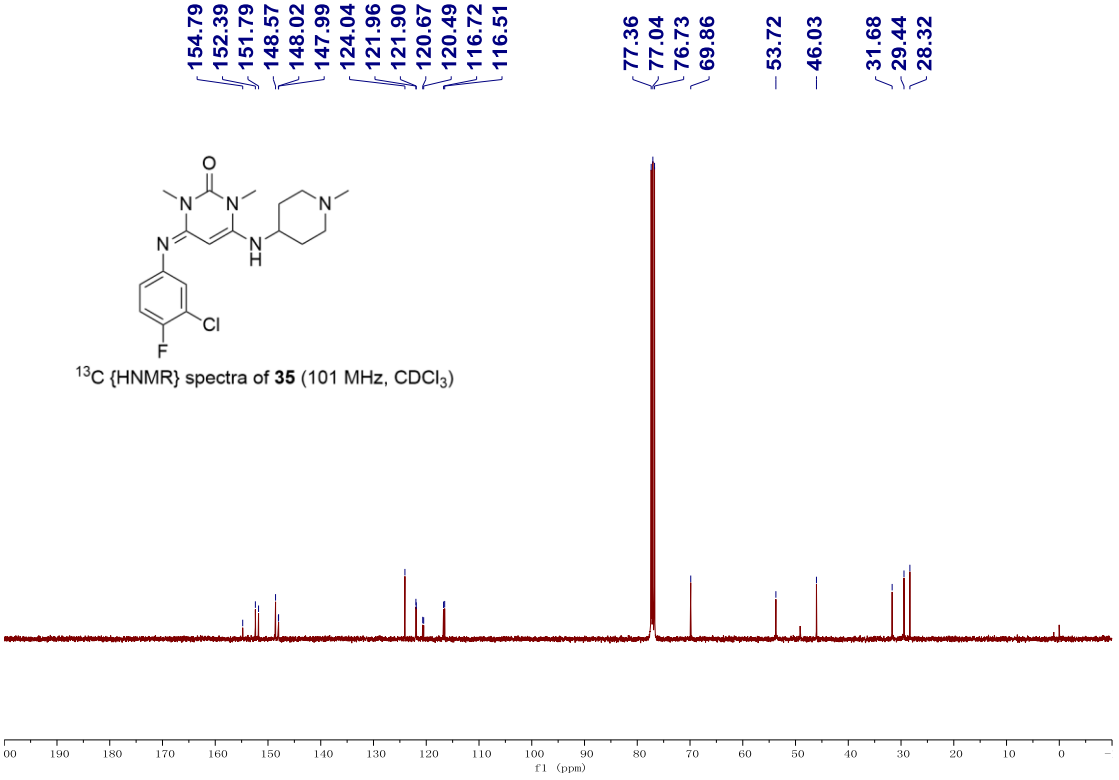


^{19}F NMR spectra of **34** (400 MHz, $CDCl_3$)

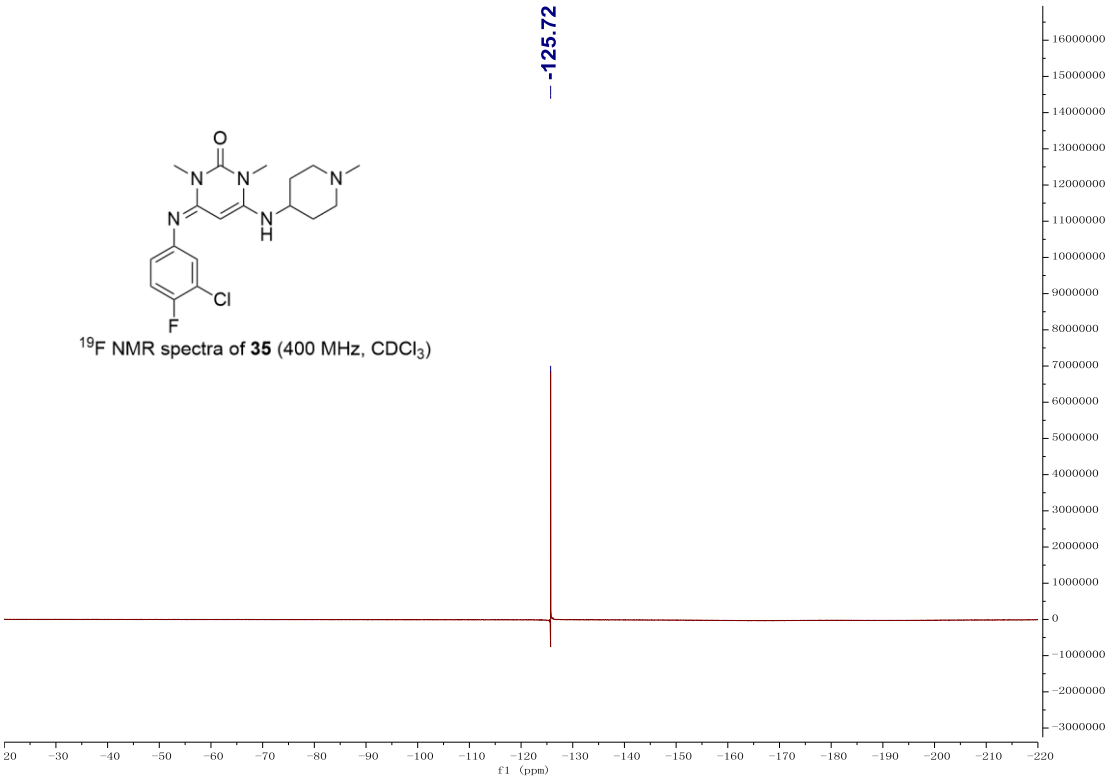




^{1}H NMR spectra of **35** (400 MHz, $CDCl_3$)

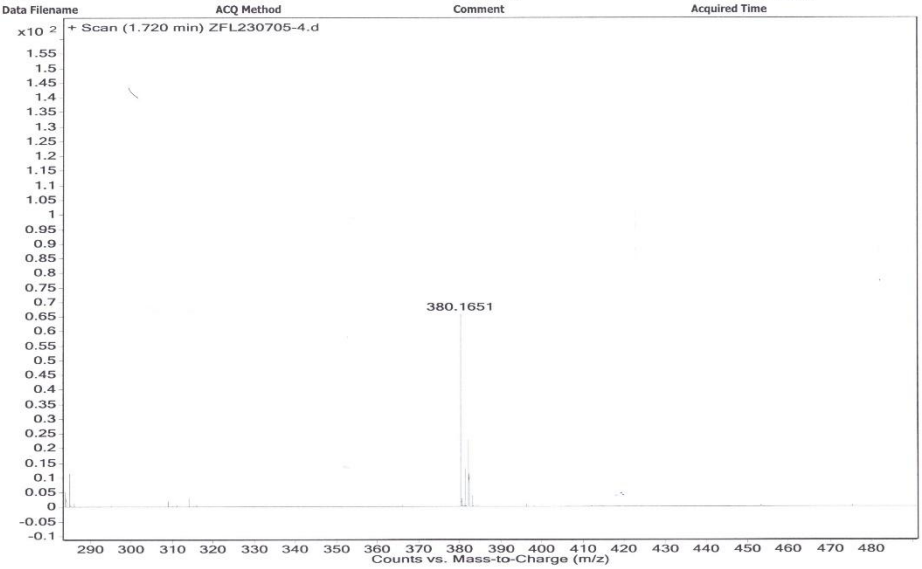


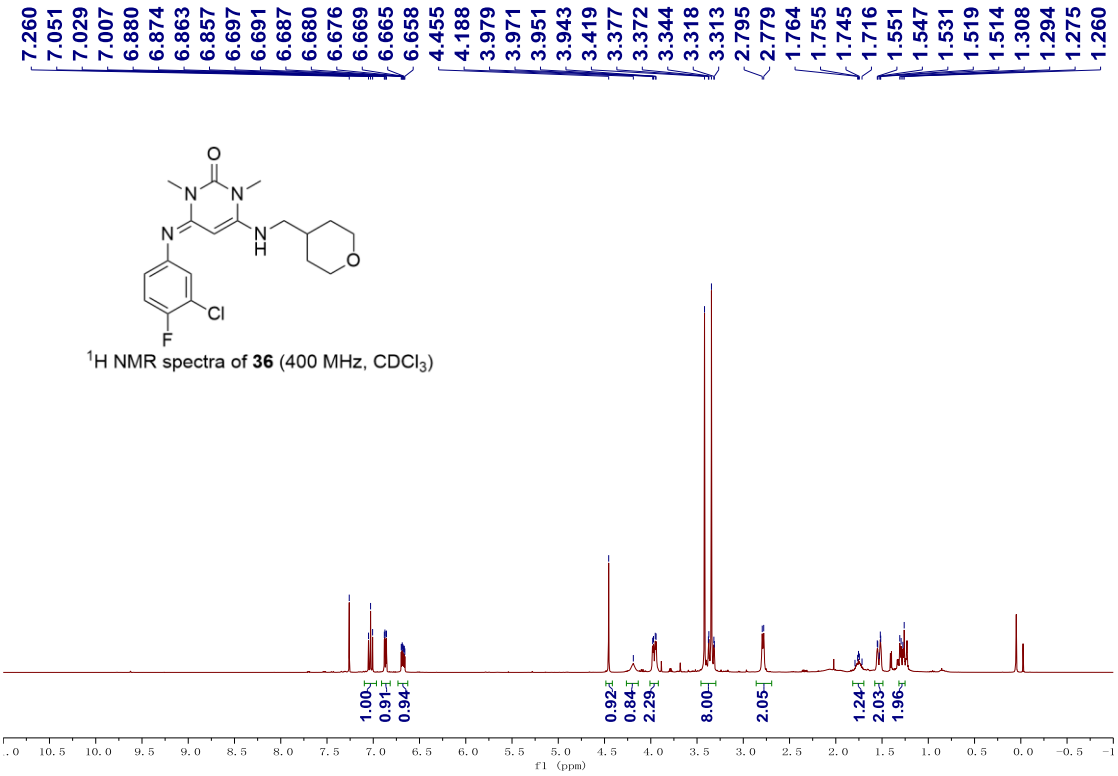
^{13}C {HNMR} spectra of **35** (101 MHz, $CDCl_3$)



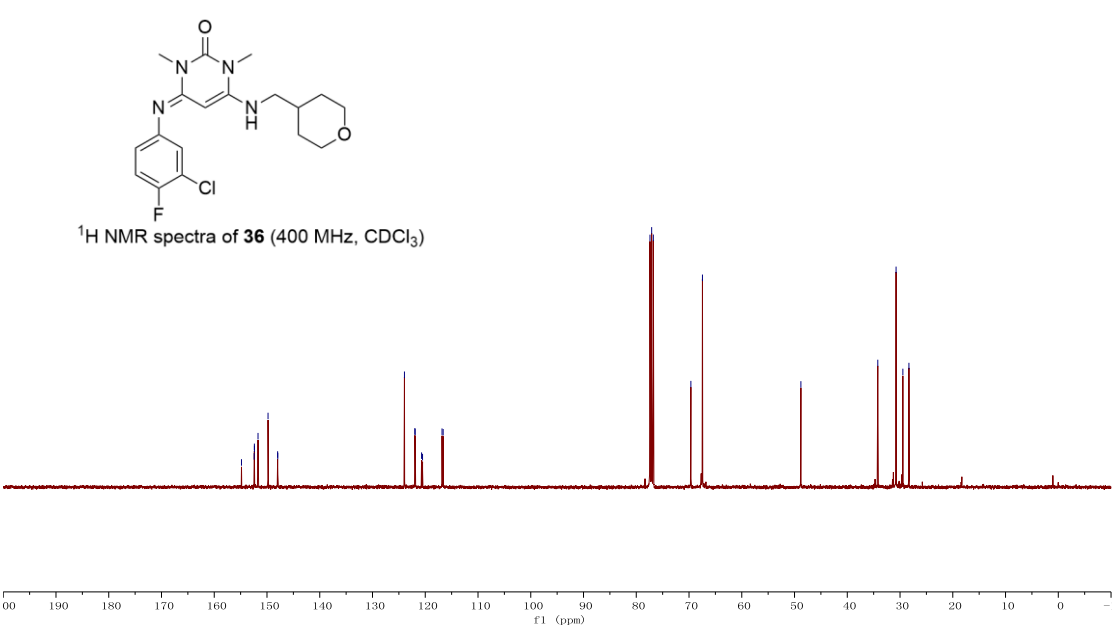
^{19}F NMR spectra of **35** (400 MHz, $CDCl_3$)

Sample Name	**Position**	**Instrument Name**	**User Name**
Inj Vol	**InjPosition**	**SampleType**	**IRM Calibration Status**
Data Filename	**ACQ Method**	**Comment**	**Acquired Time**



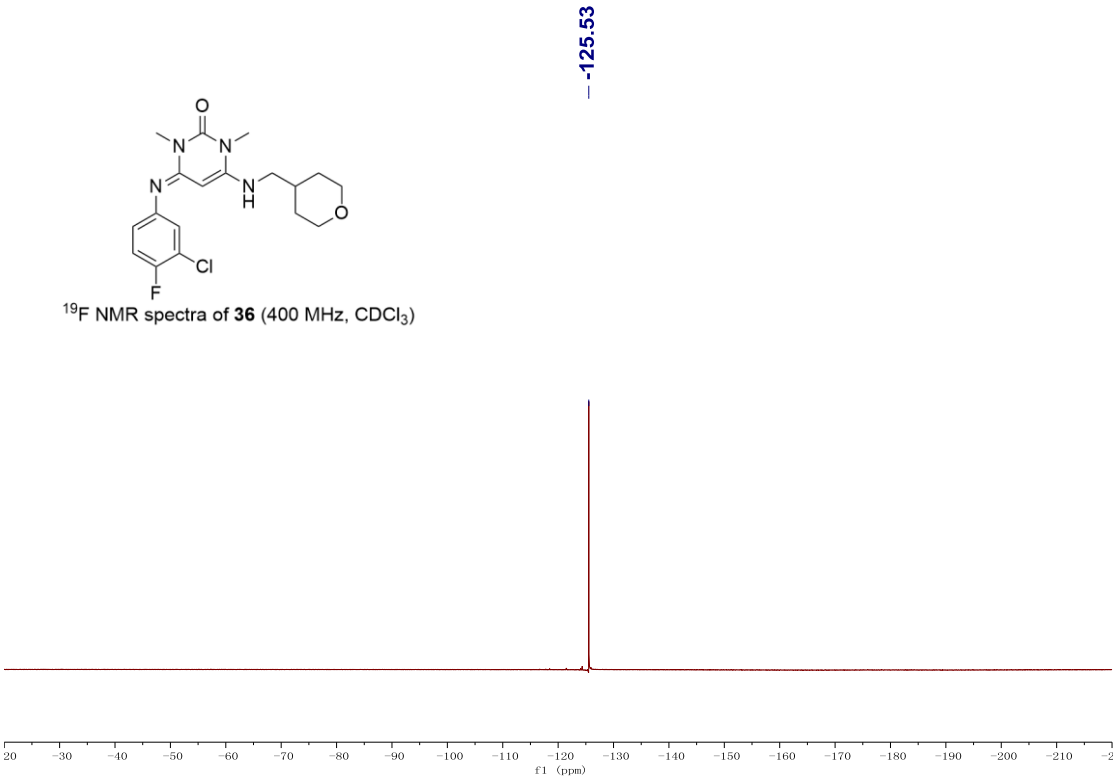


^{1}H NMR spectra of **36** (400 MHz, $CDCl_3$)



^{1}H NMR spectra of **36** (400 MHz, $CDCl_3$)

^{19}F NMR spectra of **36** (400 MHz, $CDCl_3$)



Sample Name	**Position**	**Instrument Name**	**User Name**
Inj Vol	**InjPosition**	**SampleType**	**IRM Calibration Status**
Data Filename	**ACQ Method**	**Comment**	**Acquired Time**